



Short Cases in

Clinical Medicine

6th Edition

ABM Abdullah

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Sixth Edition

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Short Cases in Clinical Medicine, 6e

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*“To study the phenomena of disease without books is to sail an uncharted sea,
while to study books without patients is not to go to sea at all”*
–Sir William Osler

Dedicated to
*My parents for their never-ending
blessings, love and encouragement*

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Preface to the 6th Edition

All praise to Almighty Allah for enabling me to bring out the 6th edition of this book. The last edition was well accepted and appreciated by a wide variety of undergraduate and postgraduate medical students from different countries. It is a difficult task to improve on the already popular version, but my sincere efforts are to incorporate the advances in medical knowledge as new texts, diagrams, tables, latest investigations and treatments, which I hope, have enriched the book.

All the chapters have been extensively revised and updated with well established format that will be easier to imbibe and memorize for the students, examinees and also the doctors. Many topics have been rewritten and some new topics have been incorporated in the light of the latest development and internationally accepted standard of care on that field. Important cardinal points are highlighted in boxes and tables, so that the readers can have a quick review.

Valuable suggestions and recommendations from renowned professors, doctors and students have helped me to raise the overall quality and acceptability of this book.

I would like to mention, as always, that this book is merely a guide to the practical approaches to a patient in examination set-up and in no way is a substitute to dealing with patients directly. To achieve the most out of this book, I would advise to take it in clinical wards and study it while working with real life patients.

There is no substitute for knowledge, and I hope, this edition will get increasing popularity and will help to serve my purpose to make good and efficient clinicians. Remember, “Machine, how much sophisticated it may be, cannot replace the tender touch of physician’s hand”.

Despite tremendous efforts to ensure adequate, correct and current information, errors and mistakes are natural. So, I would gratefully welcome and appreciate any constructive criticism, comment and corrections.



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Preface to the 1st Edition

Short cases are the most difficult part of the examination and no amount of brilliance will enable one to pass if one does not perform well in this section. It is this part where the candidates' ability to elicit and interpret the physical signs is closely scrutinized by the examiner, so chances of failure rate are very high, if this part is not performed properly.

From my experience, I feel that many candidates fail because of lack of necessary clinical competence, even they have good theoretical knowledge. Others fail because of inadequate preparation, lack of technique and poor presentation. So the only way to pass is "Continued practice in a systematic way, repeated exposure to different cases and rehearsal of presentation in front of others." Only reading a book will not replace this. With this idea, I have written this book to help the students to prepare themselves exactly in the way in any clinical examination. In such examination, the candidate needs to convey the impression that he is competent. I hope that this book will help to promote such an approach.

It has been divided in different chapters. Each of the short cases is also divided and described in the following way- instruction by the examiner, presentation of the case in front of the examiner and a brief discussion with relevant questions.

I think that learning and acquiring skill in short cases will be enhanced if this book is used soon after examining a patient. This will also encourage the candidate to practice with classical clinical features of the patients. I would encourage the candidates to take this book to the ward and practice during examination of the patient in a systematic way. I would also advise the candidates to have a group discussion with the help of this book, one should present the case in front of the others and others should ask questions etc. This will make a good practice and fluency and dexterity will be achieved.

Postgraduate students studying in FCPS, MD, MRCP, FRACP or other equivalent examinations in internal medicine should find this book very useful. It contains more than enough informations for the undergraduate students also.

It should also be remembered that short cases are also an important milestone for a good and practicing physician.

I do not claim that this book is adequate enough for whole clinical medicine and one should consult other standard textbooks. I would invite constructive criticism from the valued readers of this book, so that any errors or omission may be corrected.

I pay my humble respect to my teacher Professor M A Quaderi, FRCP (London), FRCP (Glasgow), FCPS (BD), Vice-Chancellor, Bangabandhu Sheikh Mujib Medical University and Ex-Professor of Medicine, Dhaka Medical College & Hospital and Institute of Postgraduate Medicine & Research, whose continuous encouragement and support helped me to prepare this book.

I sincerely acknowledge my debt to my teacher Professor Muniruddin Ahmed, FRCP (Glasgow), FRCP (London), Ex-Professor of Medicine, Dhaka Medical College & Hospital for his inspiration, guidance and constructive criticism and corrections in preparing the manuscript of this text.

I am grateful to Professor M N Alam, FRCP (Glasgow), FCPS (BD), Professor of Medicine, Bangabandhu Sheikh Mujib Medical University, for his valuable suggestions and encouragement in writing this book.

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Last, but not the least, I would like to express my gratitude to my wife, whose untiring support and sacrifice has made it possible to bring out such a nice book. I am also grateful to my daughter Dr. Sabah and my son Dr. Sadi for their encouragement and inspiration in preparing such a book.

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GENERAL EXAMINATION

1

'Doctors must be good observants like detectives'
—Author's View

INTRODUCTION

During examination of a short case, examiner usually asks to examine a particular part of the body or sometimes the whole system or whole body. Candidate should prepare himself to examine accordingly, but systematically. Common instructions by the examiner are:

1. General examination:

Perform the general examination of this patient. Or look at the patient or look at the face or look at the legs etc. What are your findings? What is the likely diagnosis?

2. Cardiovascular system (CVS):

- Examine the precordium. Or look at the precordium, what are your findings?
- Palpate and auscultate the precordium.
- Examine the pulse.
- Examine the CVS.

3. Respiratory system:

- Examine the chest (front or back or both).
- Auscultate the chest (front or back or both).
- Percuss and auscultate the back of chest.

4. Abdomen:

- Examine the abdomen.
- Look at the abdomen. What are the findings?
- Palpate the abdomen and relevants.
- Examine the gastrointestinal system.

5. Neurology:

- Examine the lower limbs or upper limbs.
- Examine the cranial nerves or a particular cranial nerve (e.g., facial nerve).
- Examine for cerebellar signs. Or show the reflex, rigidity, sensory test.
- Look at the gait of the patient.
- Look at the patient (If any gross finding e.g., tremor, chorea, dystonia).
- Talk with the patient (e.g., dysphasia, aphasia, hoarseness).

6. Endocrinology:

- Examine the neck (usually for goitre).
- Examine the thyroid gland and relevant features (Goitre, features of hyper or hypothyroidism).
- Look at the face (e.g., in thyrotoxicosis, myxoedema, acromegaly or Cushingoid, hirsutism).
- Perform the general examination (e.g., obesity, features of myxoedema, pigmentation in Addison's disease).
- Look at the patient (e.g., may be short or long stature), also see the relevant features.

7. Rheumatology:

- Examine the hands (e.g., rheumatoid hand, systemic sclerosis).
- Examine the knee joints (or any particular joint e.g., monoarthritis, polyarthritis, effusion in knee joints).
- Examine the face and relevant features (e.g., systemic sclerosis, systemic lupus erythematosus, dermatomyositis).
- Look at the skin (dermatomyositis, psoriatic arthritis).
- Look at the patient and examine the relevant features (e.g., ankylosing spondylitis).

8. Dermatology:

- Perform the general examination (e.g., psoriasis, exfoliative dermatitis).
- Look at the skin. What are the findings? (e.g., skin rash, erythema multiforme, purpura, Stevens Johnson syndrome, blisters).
- Look at the face. What are the findings? (e.g., butterfly rash, PKDL, leprosy, pigmentation).

9. Eyes:

- Examine the eyes or look at the eyes (e.g., xanthelasma, ptosis, squint, pigmentation of sclera, **Kayser–Fleischer** ring, corneal arcus, subconjunctival haemorrhage, exophthalmos, pupil, movement of eyeball).
- Perform fundoscopy (e.g., optic atrophy, papilloedema, retinopathy, retinal haemorrhage).

10. Miscellaneous:

Depends on a particular type of case, e.g., Turner's syndrome, Down's syndrome, xanthelasma etc.

- Look at the tongue. What is the diagnosis? What are the diseases that can be diagnosed by looking at the tongue?
- Look at the face. What is your diagnosis? Name some diseases that can be diagnosed by looking at the face.
- Examine the hands. What is your diagnosis? What are the diseases that can be diagnosed by examining the hands? Or by hand shake?
- Look at the nails. What is your diagnosis? What diseases are diagnosed by looking at the nail?



Cachexia



Pallor of palm



Jaundice



Clubbing



Koilonychia



Leukonychia



Pitting oedema



Non-pitting oedema



Pigmentation



Goitre



Lymphadenopathy



Alopecia

PHYSICAL EXAMINATION

Before starting the examination, ideally the patient should be made to lie comfortably on bed. Clothes should be removed with permission, use pillows or backrest for patients who are breathless in flat position. Take few moments to look quickly from head to foot (keeping open your **wide-angled lens**), by which some clue to the diagnosis may be obvious (such as emaciation or cachexia, obesity, acromegaly, myxoedema, thyrotoxicosis, Cushing's syndrome, kyphosis, scoliosis, lordosis).

Be sure that you are on the right side of the patient. Introduce yourself, be gentle and polite. With permission, tell the patient, 'I am Dr . . . , I would like to examine you. Would you please allow me to do so? Please tell me, if I hurt you'. A friendly handshake may offer patient's reassurance and co-operation, also may help to get information such as warm and sweaty hands (**thyrotoxicosis**), cold and sweaty hands (**anxiety**), dry and coarse hands (**hypothyroidism**), doughy feeling (**acromegaly**) and slow relaxation of hand grip (**myotonia**).

Look at the face, some diseases may be diagnosed by the **facial expression of the patient** (for details, see pages 512, 601, 672, 881), for example:

- Mask-like face (in Parkinsonism).
- Agitated or terror face (in thyrotoxicosis).
- Exophthalmos (in Graves' disease).
- Puffy face (in myxoedema or nephrotic syndrome).
- Apathy (in depression).

Look at the **height**—Tall or short (see below).

GENERAL EXAMINATION:

- **Appearance** (ill-looking, depressed, anxious, Cushingoid or expressionless face).
- **Built** (obese, emaciated or cachexic, tall, short or normal).
- **Nutrition** (well nourished, poor or normal).
- **Co-operation.**
- **Decubitus** (on choice, propped up or Mohammedan prayer position).
- **Anaemia** (see in palpebral part of conjunctiva, tongue, palm, nails and whole body).
- **Jaundice** (see in sclera, under surface of tongue, palm or whole body).
- **Cyanosis** (see in tip of nose, lips, ear lobule, tongue, tip of fingers and toes).
- **Clubbing** (see fluctuation of nail base, angle between the nail and its base, curvature of nails, look for hypertrophic osteoarthropathy by pressing the lower end of tibia, fibula or radius, ulna).
- **Koilonychia** (see dryness, brittleness, flattening, thinning and spooning of nails).
- **Leukonychia** (white spots or white nail).
- **Oedema** (see in leg above medial malleolus, sacrum if the patient is recumbent).
- **Dehydration** (see skin turgor or dry tongue).
- **Pigmentation** (see in exposed parts, face, neck, palmar creases, knuckles, inner side of mouth or recent scar).
- **Lips, tongue, oral mucosa, nose.**
- **Lymph nodes** (examine systematically in different areas).
- **Thyroid gland** (if enlarged, examine in detail and see the features of toxicosis or hypothyroidism).
- **Breasts (to see gynaecomastia or lipomastia).**
- **Body hair distribution** (including head to see alopecia).
- **Neck veins.**
- **Pulse.**
- **Blood pressure.**
- **Temperature.**
- **Respiratory rate.**

N.B.: If obvious other findings are present, those should be mentioned (that indicates certain particular disease).

During routine general examination, some extra findings in individual cases should be seen if present. For example:

- In Cushing's syndrome: some extra findings must be seen e.g., striae, moon face and buffalo hump.
- If butterfly rash is seen on the face: check for rash in other parts of the body. Also, heliotrope rash and alopecia.
- If suspicion of CLD, look for the stigmata of CLD.

Relevant findings should be examined according to individual cases, for example:

1. In the face:

If xanthelasma is present, see corneal arcus, xanthomatous nodules in others parts (elbow, knees, extensor surfaces, Achilles tendon and palmar creases).

2. In the hands:

- Dupuytren contracture.
- Palmar erythema.
- Osler node and splinter haemorrhage (in subacute bacterial endocarditis).
- Heberden node.
- Bouchard node.
- Gangrene or nail fold infarct or nail fold telangiectasia.
- Ulceration.
- Wasting.
- Skin rash or Gottron patch (dermatomyositis).

3. Other findings:

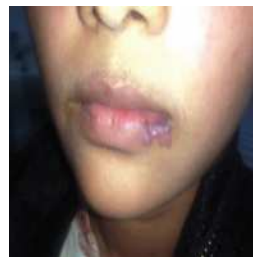
- Spider angioma.
- Parotid gland enlargement (unilateral or bilateral).
- Skin rash.
- Striae.
- Campbell de Morgan spots.
- Purpura.
- Vitiligo.
- Deformity (kyphosis, scoliosis and lordosis).



Gynaecomastia



Dupuytren's contracture



Herpes Labialis



Multiple sinuses (TB)

N.B. Remember the following points:

- *Mention, if the patient has any cannula, catheter, NG tube, CV line, AV fistula etc.*
- *Never forget to examine the lower limbs (there may be unilateral leg swelling, deep vein thrombosis, differential cyanosis, differential clubbing, trophic ulcer, gangrene or infarction at the tip of toes).*

After examination is complete, present the case to the examiner systematically. Remember, you must follow the examiner's instructions. For example, examiner may ask:

- What are your findings? (Mention the positive and important negative findings).
- Have you finished your examination? Now tell your findings (Mention accordingly).

EXAMPLES OF PRESENTATION OF A CASE

Case No. 1 (Cachexic Patient):

- The patient is ill-looking, emaciated or cachexic with poor nutrition. He/she is mildly anaemic, no jaundice, no cyanosis.
- There is clubbing involving all the fingers and toes, no leukonychia and no oedema.
- Thyroid gland is normally palpable and there is no lymphadenopathy.
- He/she is normally pigmented.
- Pulse: 80/min.
- Neck veins: are not engorged.
- BP: 120/8 mmHg, respiration: 18/min and temperature: normal.

Examiner may ask:

Q: What are the **causes of cachexia** in this elderly patient?

A: Tuberculosis, diabetes mellitus, thyrotoxicosis, malignancy, malnutrition or malabsorption.

Q: What **investigation** would you suggest in this case?

A: I will take the details history and investigate accordingly e.g., Chest X ray, Blood sugar etc.

Q: What are the **causes of cachexia** in this young lady?

A: Tuberculosis, diabetes mellitus, thyrotoxicosis, malnutrition or malabsorption, anorexia nervosa, Addison's disease.

Q: What are the **causes of clubbing** in this case?

A: See later in the topic 'clubbing'.

Q: If the patient has **goitre**, what history would you like to take?

A: Appetite, heat intolerance, weight loss.

Case No. 2 (Obese Patient):

- This patient is obese, mildly anaemic, no jaundice, no cyanosis, no clubbing, koilonychia or leukonychia. No other abnormalities are present.

Examiner may ask:

Q: What are the **causes of obesity**? What **else** do you like to see in obesity?

A: I want to look for striae, central obesity, moon face and buffalo hump (in Cushing's syndrome).
For details, see in the topic 'obesity'.

Case No. 3 (Generalized Lymphadenopathy):

- The patient has generalized lymphadenopathy (involving . . . , which are of variable size and shape, some are firm and some are soft, discrete, nontender, not fixed with overlying skin or underlying structure).

Examiner may ask:

Q: What are the **causes of generalized lymphadenopathy**? How will you **investigate**?

A: For details, see in the topic lymphadenopathy.

Case No. 4 (Tall Stature):

- The patient is tall, lean and thin.

Examiner may ask:

Q: What are your **findings**?

A: The patient is tall, lean and thin. Extremities are long, face is narrow and elongated with arachnodactyly (long, elongated fingers)—likely to be a case of **Marfan's syndrome**.

Q: What **else** do you like to examine?

A: I want to examine the eyes (dislocated lens), heart (aortic regurgitation), high-arched palate, arm span and height.

Case No. 5 (Tall and Obese):

- The patient is tall and obese.

Examiner may ask:

Q: What are your **findings**? What **else** do you want to see?

A: The patient is tall and obese. I want to see gynaecomastia, testis (atrophy), secondary sex characters and voice. This may be a case of **Klinefelter's syndrome**.

Case No. 6 (Generalized Pigmentation):

- This young patient has generalized pigmentation.

Examiner may ask:

Q: What are your findings? What else do you want to see?

A: There is generalized pigmentation. I want to see—BP, both standing and lying position to see postural hypotension (blood pressure is low in Addison's disease, also postural hypotension). Also I want to see pigmentation in other parts of the body (such as inner side of mouth, palmar crease, recent scar).

Case No. 7 (Generalized Oedema):

- The patient has generalized oedema which is pitting in nature.

Examiner may ask:

Q: What are the possibilities? What else do you want to examine?

A: There is generalized oedema, which may be due to nephrotic syndrome, hypoproteinaemia, cirrhosis of the liver etc. (For details, see the relevant topics later in the respective chapters.)

READ THE FOLLOWING TOPICS IN GENERAL EXAMINATION

Decubitus:

- Propped up position—Usually in acute LVF, Respiratory distress (Acute severe asthma) etc.
- Mohammedan prayer position—Usually in Acute pancreatitis.
- Head retraction or extended neck indicates acute meningitis.

Causes of tall stature:

- Normal, constitutional.
- Gigantism.
- Marfan's syndrome
- Klinefelter's syndrome
- Eunuchoidism

Causes of short stature:

- Constitutional
- Familial
- Genetic—Down's syndrome, Turner's syndrome, Achondroplasia, Cystic fibrosis.
- Endocrine—Cretinism or juvenile hypothyroidism, Hypopituitarism
- Any chronic illness from childhood—Nutritional, Cardiac, Renal etc.

Causes of Pallor (Face or Whole Body):

1. Anaemia (the commonest cause). For details, see in the chapter Haematology.
2. Hypopituitarism (or hypogonadism).
3. Others (Usually acute):
 - Shock.
 - Syncope.
 - Left ventricular failure.



Propped up position



Mohammedan's Prayer Position



Tall stature



Short stature

Causes of Yellow Body:

- Jaundice (the commonest cause).
- Carotenaemia.

Causes of Carotenaemia:

- Excess intake of carotene-containing food (carrot, mango and tomato).
- Hypothyroidism (due to impaired metabolism of carotene by liver).

Q: How to differentiate between jaundice and carotenaemia?

A: In jaundice, sclera is involved. In carotenaemia, sclera is not involved, only other parts of the body are involved.

Causes of shallow brown discoloration: CKD.

Causes of red discoloration: Clofazimine therapy.

Causes of cherry-red discoloration of skin: Carbon monoxide poisoning.

JAUNDICE



Jaundice in sclera



Jaundice in body



Jaundice in palm

Q: What is jaundice? Why upper sclera is seen in jaundice?

A: It is a clinical condition characterized by yellow discolouration of skin and mucous membrane due to excess bilirubin in the blood. Clinically, jaundice is seen when serum bilirubin is >3 mg/dL. If it is <2.5 mg/dL, called subclinical (or anicteric hepatitis). Jaundice should be seen in natural daylight. Bilirubin has strong affinity for elastic tissue, sclera contains plenty of elastic tissue (also in the skin). So, it is seen in sclera.

Q: What are the types of jaundice?

A: Jaundice is 3 types:

1. Prehepatic (predominantly unconjugated hyperbilirubinaemia).
2. Hepatocellular (both conjugated and unconjugated hyperbilirubinaemia).
3. Posthepatic or obstructive (predominantly conjugated hyperbilirubinaemia).

Q: What are the causes of jaundice?

A: Causes of jaundice: Varies according to types.

A. Causes of Prehepatic jaundice:

1. Excess production of bilirubin (due to breakdown of RBC)—It is found in haemolytic anaemia due to any cause.
2. Reduced hepatic uptake of bilirubin or impaired conjugation:
 - Gilbert syndrome.
 - Drugs—sulphonamides, penicillin, rifampicin.
 - Crigler–Najjar syndrome Type 1 and 2.
 - Physiological jaundice of newborn.

B. Causes of Hepatocellular jaundice:

1. Viral hepatitis due to A, B, C, D, E, other virus such as EBV, CMV, Yellow fever, dengue, (Nonviral infections e.g., leptospirosis, Q fever).
2. Drugs—Antitubercular drugs (rifampicin, pyrazinamide, INH), Phenothiazines (chlorpromazine, haloperidol), Cyclosporine, Alcohol.
3. Metabolic—Wilson's disease, haemochromatosis.
4. Autoimmune hepatitis.
5. Inherited disorders (Dubin–Johnson syndrome, Rotor syndrome).

C. Causes of Posthepatic or Obstructive jaundice:**1. Extrahepatic:**

- Choledocholithiasis.
- Carcinoma of head of pancreas.
- Cholangiocarcinoma.
- Periapillary carcinoma.
- Extrahepatic biliary atresia.
- Round worm in common bile duct.
- Biliary stricture (due to trauma, sclerosing cholangitis).

2. Intrahepatic:

- Primary biliary cirrhosis (PBC).
- Primary sclerosing cholangitis.
- Viral hepatitis (causes transient intrahepatic cholestasis).

Q: What are the types of **congenital non-haemolytic hyperbilirubinaemia**?

A: 4 types:

- Gilbert's syndrome (Unconjugated).
- Crigler–Najjar syndrome (Unconjugated).
- Dubin–Johnson syndrome (Conjugated).
- Rotor's syndrome (Conjugated).

Q: This patient has jaundice. What **history** should be taken?

A: History to be taken in a jaundice patient:

- Anorexia, nausea and vomiting (indicates viral or drug induced hepatitis).
- Colour of the stool (yellowish, pale, dark), itching indicates obstructive jaundice.
- Family history of jaundice, consanguinity of marriage among parents, associated with pallor (indicates hereditary haemolytic anaemia, in prehepatic jaundice).
- History of contact with jaundiced patient or sexual exposure.
- History of injection, infusion or blood transfusion, I/V drug abuse, tattooing or surgery (HBV or HCV).
- History of travelling abroad (hepatitis B).
- History of possible contaminated food, water, milk, other items.
- History of alcohol or any drugs.
- Associated history of high fever, urinary complain (indicates leptospirosis).
- Recurrent jaundice associated with any neurological abnormality (indicates Wilson's disease).
- Associated abdominal pain and fluctuating jaundice (indicates bile duct stricture or stone).

Q: What are the **common features** of different types of jaundice? How to **investigate**?

A: Features of different types of jaundice:

Features of prehepatic jaundice—

- Usually in hereditary haemolytic anaemia. There is triad of anaemia, jaundice and splenomegaly. Other features—frontal and parietal bossing, mongoloid facies.
- Other features are according to the causes of haemolytic anaemia—malaria, autoimmune haemolytic anaemia.

Features of hepatocellular jaundice—

- Anorexia, nausea, vomiting, weakness.
- Stool is yellow (but may be dark or clay coloured in later stage due to intrahepatic cholestasis).
- Liver is enlarged and tender.

Features of obstructive jaundice—

- Pale, dark or clay coloured stool.
- Itching of whole body.
- May be abdominal pain, mass in the epigastrium.
- Other features depend upon cause (xanthelasma or xanthoma in PBC).
- Bleeding tendency (due to deficiency of Vitamin K, resulting in deficiency in Vitamin K dependent clotting factors— II, VII, IX, X).
- Bone pain (due to osteomalacia).

Investigations in jaundice:

1. Liver function tests such as serum bilirubin, SGPT, SGOT, alkaline phosphatase, prothrombin time.
2. USG of hepatobiliary system.
3. Viral markers:
 - For A—anti-HAV IgM.
 - For E—anti-HEV IgM.
 - For B—HBsAg, HBeAg, anti-HBc.
 - For C—anti-HCV.
4. Other investigation should be done according to the suspicion of cause. Such as:
 - For haemolytic anaemia—Hb electrophoresis
 - In obstructive jaundice—ERCP, MRCP.
 - CT scan of whole abdomen.

Treatment:

1. General measures: See in the respective chapters.
2. Specific: According to the cause.

READ THE FOLLOWING TOPICS IN JAUNDICE

Causes of fluctuating jaundice:

- Choledocholithiasis.
- Choledochal cyst.
- Sometimes in primary sclerosing cholangitis.
- Haemolytic jaundice.
- Wilson disease.
- Gilbert's syndrome.
- Benign recurrent intrahepatic cholestasis (BRIC).
- Recurrent pancreatitis.

Causes of progressive jaundice:

- Acute viral hepatitis.
- Carcinoma of the head of the pancreas.
- Cholangiocarcinoma.
- Primary biliary cirrhosis.
- Primary sclerosing cholangitis.

Causes of recurrent jaundice:

- Congenital hyperbilirubinaemia (e.g., Gilbert syndrome).
- Recurrent benign cholestasis.

Causes of palpable gall bladder with jaundice:

- Carcinoma of head of pancreas.
- Carcinoma of ampulla of Vater.
- Stone in common bile duct.
- Pressure from outside on bile duct (lymphoma and secondaries).
- Cholangiocarcinoma.
- Sclerosing cholangitis.

Causes of palpable gall bladder without jaundice:

- Mucocoele.
- Empyema.
- Occasionally, carcinoma of the gall bladder.

Causes of painless progressive jaundice with palpable gallbladder:

- Carcinoma of head of the pancreas.

Causes of abdominal pain with fluctuating jaundice:

- Stone in CBD or stricture.
- Pancreatitis.

Causes of jaundice with itching:

- Obstructive jaundice
- Primary biliary cirrhosis.

CYANOSIS



Cyanosis in toe



Cyanosis in nail



Cyanosis at tip of nose and lips

Definition: It is the bluish discolouration of skin and mucous membrane due to increased amount of deoxygenated haemoglobin in the blood. Cyanosis is not seen until the amount of deoxygenated haemoglobin is >5 gm%.

Types of cyanosis: It is of 2 types—

1. **Peripheral:** Due to localized reduction of blood flow on exposure to cold causing capillary vasoconstriction (lip is blue in cold weather). Also, occurs in reduced cardiac output (heart failure or shock). Tongue is spared in peripheral cyanosis. Causes are:
 - Exposure to severe cold, frostbite.
 - Raynaud's phenomenon.
 - Heart failure.
 - Shock and peripheral circulatory failure.
 - Deep vein thrombosis.
 - Cryoglobulinaemia.
2. **Central:** Either due to imperfect oxygenation of blood in lung or admixture of venous and arterial blood. It is evident when O_2 saturation falls below 80 to 85%. Best site to see is tongue. Causes are:

Respiratory: There is defect in oxygenation of blood in the lungs:

- Chronic obstructive pulmonary disease (COPD).
- Severe pneumonia.
- Tension pneumothorax.
- Massive lung collapse.
- Acute severe bronchial asthma.
- Massive pulmonary embolism.
- Pulmonary infarction.
- Diffuse parenchymal lung disease (DPLD).
- Adult respiratory distress syndrome.
- Respiratory failure due to any cause.

Cardiac:

- Cyanotic congenital heart disease: Fallot's tetralogy, transposition of great vessels.
- Shunt anomaly (reversal of shunt, right-to-left shunt called Eisenmenger syndrome), causes are: atrial septal defect, ventricular septal defect, patent ductus arteriosus.
- Acute left ventricular failure.
- Cardiogenic shock.

Others:

- High altitude (physiological).
- Polycythaemia.

Q: What are the **differences** between central and peripheral cyanosis?

A: As follows:

Points	Central	Peripheral
1. Mechanism	Imperfect oxygenation of blood in lung or admixture of venous and arterial blood in heart disease.	Local vasoconstriction or reduction of arterial flow.
2. Cyanosis	Generalized	Localized
3. Affected part	Warm	Cold
4. Application of warm	Does not disappear	Disappears
5. Oxygen	Cyanosis may disappear in pulmonary case (except in right-to-left shunt)	Disappears
6. Tongue	Always involved	Never involved

Q: Why **tongue** is not involved in peripheral cyanosis?

A: Because tongue is always warm and circulation is good in tongue.

Q: Why there is **no cyanosis** in severe anaemia?

A: Because in severe anaemia, Hb is low and fully saturated, so there is no deoxygenated Hb (deoxygenated haemoglobin should be >5 gm% for cyanosis to be evident). In polycythaemia, cyanosis may occur even in mild hypoxia.

Q: What is **enterogenous** cyanosis? How to **diagnose**?

A: Discolouration of skin due to the presence of abnormal pigments in blood. It occurs in sulphaemoglobinaemia or methaemoglobinaemia. There may be history of intake of some drugs (sulphonamide, phenacetin and dapsone). No dyspnoea in enterogenous cyanosis or no other respiratory symptoms. This can be diagnosed by spectroscopic examination of blood.

CLUBBING

Instruction by the examiner:

- Perform the general examination of this patient.
- Examine the hands or look at the fingers. What are your findings?



Fluctuation test



Schamroth sign



Clubbing of all fingers

Proceed as follows:

- First look whether gross clubbing is present or not.
- If not, look carefully at the angle between nail and its base at the level of the observer's eye (normal angle is 160°).
- Next, see the fluctuation at the nail bed.
- Place the corresponding opposite nails of both hands (normally, small gap is present. If clubbing, there is reduction or absence of the gap, called window sign or Schamroth sign).
- Look to see the convexity of nails from side-to-side.
- In advance stage—drumstick or parrot-beak appearance.
- Always see hypertrophic osteoarthropathy—press the ends of long bones (radius and ulna, tibia and fibula). Look at the face (patient winces due to pain).

N.B.: You must look at both the fingers and toes.



Clubbing in toes



Drumstick appearance



Parrot beak appearance



Clubbing with cyanosis

Presentation of a Case:

- This patient has generalized clubbing involving all the fingers and toes with drumstick appearance (or parrot beak) and hypertrophic osteoarthropathy (mention, if any).

Q: What **else** do you want to examine?

A: I want to take the family history of clubbing, also I want to examine respiratory system, heart and abdomen to find out the causes.

Q: What is the **early sign** of clubbing?

A: Softening of nail bed with obliteration of the angle of nail bed.

Q: What is **Schamroth sign**?

A: When finger nails of the corresponding fingers of each hand are placed against each other, normally there is a diamond-shaped gap between them called Schamroth sign. It is lost in finger clubbing.

Q: What do you think the **causes** of clubbing in this case?

A: Tell the causes according to the age of the patient.

If the patient is middle aged or elderly, the causes are:

1. Respiratory:

- Bronchial carcinoma (commonly squamous cell type).
- Suppurative lung disease (bronchiectasis, lung abscess, empyema thoracis).
- DPLD (ILD).
- Pulmonary TB (in advanced stage with fibrosis).

2. Cardiac: Infective endocarditis (SBE).

3. Others: Cirrhosis of liver, primary biliary cirrhosis, inflammatory bowel disease, familial (rare) and idiopathic (rare).

If the patient is young or child, the causes are:

1. Respiratory:

- Suppurative lung disease (bronchiectasis, lung abscess).
- Cystic fibrosis.
- Pulmonary TB (in advanced stage with fibrosis).

2. Cardiac:

- Cyanotic congenital heart disease (Fallot's tetralogy).
- Infective endocarditis (SBE).

3. Others: Chronic liver disease (which may be due to Wilson's disease and alpha-1-antitrypsin deficiency).

N.B. Commonest cause of clubbing in elderly is bronchial carcinoma and in young is bronchiectasis.

READ THE FOLLOWING TOPICS IN RELATION TO CLUBBING

Q: What is **clubbing**?

A: It is defined as bulbous enlargement of the terminal phalanges of fingers and toes with increase in the soft tissue mass and curvature of the nails.

Q: What are the causes of clubbing? (Theoretically)**A:** As follows (common causes are related to respiratory and cardiovascular system):

1. Respiratory:
 - Bronchial carcinoma.
 - Suppurative lung disease (bronchiectasis, lung abscess, empyema thoracis).
 - DPLD (ILD).
 - Pulmonary TB (in advanced stage with fibrosis).
 - Pleural mesothelioma.
 - Pulmonary arteriovenous fistulae.
 - Cystic fibrosis.
2. Cardiac:
 - Cyanotic congenital heart disease (Fallot's tetralogy).
 - Infective endocarditis (SBE).
 - Atrial myxoma.
3. GI tract:
 - Inflammatory bowel disease (Crohn's disease, Ulcerative colitis).
 - Polyposis coli (rarely).
4. Hepatobiliary:
 - Chronic liver disease (e.g., Cirrhosis of liver).
 - Primary biliary cirrhosis.
5. Miscellaneous:
 - Familial (rare).
 - Idiopathic.
 - Congenital.
 - Thyrotoxicosis (called thyroid acropachy).

Q: What history should be taken in clubbing?**A:** As follows:

- Family history.
- Respiratory problem such as cough, haemoptysis, chest pain, breathlessness.
- Cardiac such as history of cyanotic congenital heart disease, history suggestive of infective endocarditis.
- Gastrointestinal tract such as diarrhoea, bloody diarrhoea (IBD).
- History of liver disease.

Q: What is differential clubbing? What are the causes?**A:** It means clubbing in the toes, but not in the fingers or clubbing in the fingers not in the toes.

Causes of clubbing in toes (not in fingers):

- PDA with reverse shunt (also there is cyanosis in toes, not in finger called differential cyanosis).
- Infected abdominal aortic aneurysm.
- Coarctation of abdominal aorta.

Causes of clubbing in fingers (not in toes):

- Chronic obstruction of veins (phlebitis) of upper extremities (common in IV drug abusers).

Q: What are the causes of **unilateral** clubbing?

A: As follows:

- Pre-subclavian coarctation of aorta.
- Arteriovenous fistulae of brachial vessels.
- Aneurysm of subclavian artery.
- Pancoast tumour.
- Erythromelalgia.

Q: What are the **causes of** clubbing of single finger? (unidigital clubbing)

A: As follows:

- Repeated local trauma (commonest cause).
- Chronic tophaceous gout.
- Sarcoidosis.
- Median nerve injury.

Q: What are the **causes of** clubbing with cyanosis?

A: As follows:

- DPLD (ILD).
- Cyanotic heart disease (Fallot's tetralogy).
- Eisenmenger's syndrome.
- Cystic fibrosis.
- Bilateral extensive bronchiectasis.

Q: What is **pseudoclubbing**? What are the **causes**?

A: It means, fingers or toes look like clubbing, but there is no soft tissue proliferation or increased curvature of the nails. It is due to resorption of subperiosteal bone of terminal phalanges. Causes are:

- Systemic sclerosis.
- Hyperparathyroidism.

Q: What are the **grades or stages of** clubbing?

A: 4 stages:

- Grade 1: Softening of nail bed (fluctuation is positive). It is due to proliferation of cells at nail base.
- Grade 2: Increased curvature of nails, which become convex and angle between the nail and its base is obliterated.
- Grade 3: Increase pulp tissue, resulting in drumstick or parrot beak or both.
- Grade 4: Hypertrophic osteoarthropathy.

Q: What are the **pathogeneses or mechanisms of** clubbing?

A: Actual mechanism is unknown. Possible hypotheses are:

- Arterial hypoxaemia.
- Toxic, as in SBE.
- Humoral substances that cause vasodilatation (bradykinin, prostaglandins, 5-hydroxytryptamine).
- Neurogenic factors through vagal stimulation (vagotomy revert clubbing in some cases).
- Platelet-derived growth factor (PDGF) released from megakaryocyte and platelet emboli in nail bed, which causes increased capillary permeability, fibroblastic activity and arterial smooth muscle hyperplasia in the nails resulting in clubbing.
- Tumour necrosis factor has been implicated.

Q: Is clubbing **reversible** by any therapy?

A: Clubbing may be reversible, rarely by vagotomy (in idiopathic or familial clubbing).

Q: What **investigations** should be done in clubbing?

A: As follows:

- Full blood count.
- Chest X-ray.
- USG of whole abdomen.
- Echocardiography.
- Other—according to cause (barium enema, follow through, colonoscopy for inflammatory bowel disease, liver function test).

Q: What is **Hypertrophic Osteoarthropathy**?

A: Hypertrophic osteoarthropathy (HOA) is the **triad** of clubbing, arthritis and subperiosteal new bone formation (periosteal inflammation at the distal ends of long bones in radius, ulna, tibia, fibula, although any bone may be involved). There is swelling and tenderness at the lower ends of forearm and leg. Clubbing is usual, but not invariable in HOA (rarely occur without HOA). HOA may be primary or secondary to any cause of clubbing. Commonest causes of HOA are bronchial carcinoma (squamous cell type) and pleural mesothelioma.

Treatment of primary cause should be done. For pain, NSAID may be given.

Primary hypertrophic osteoarthropathy: It is also called pachydermoperiostosis. Usually begins in childhood or puberty, inherited as autosomal dominant, more in male. There is thickening of the skin of face and scalp, which is greasy, pigmented, furrowed forehead giving rise to 'Leonine facies'. Excessive sweating especially of palm and sole. Marked clubbing is present and distal extremities are large and thick, like elephant feet (large feet, confuses with mucopolysaccharidoses).



Pachydermoperiostosis



Thickening of sole



Thickening of palm

KOILONYCHIA

Instructions by the examiner:

- Perform the general examination.
- Look at the nail. What is your diagnosis?

Presentation of a Case:

- The patient is severely anaemic with koilonychia involving all the nails of fingers and toes, tongue is smooth, shiny with atrophy of papillae.

Diagnosis is **severe anaemia with koilonychia** (due to iron deficiency anaemia).

READ THE FOLLOWING TOPICS IN RELATION TO KOILONYCHIA

Q: What are the **causes** of koilonychia?

A: As follows:

1. Iron deficiency anaemia (commonest cause).
2. Others (rare, **better do not mention** until asked):
 - Trauma (rarely in garage mechanics, who regularly fit tyres).
 - Thyrotoxicosis.
 - Fungal infection.
 - Raynaud's disease.

Q: What is **koilonychia**? What is the **mechanism** of koilonychia?

A: It is characterized by concave or spoon shaped nail. Mechanism is unknown, probably due to slow growth of nail plate.

Q: What are the **stages** of koilonychia?

A: 3 stages—

- Stage 1—Dryness, brittleness and ridging.
- Stage 2—Flattening and thinning.
- Stage 3—Spoonng or concavity.

Q: What **else** do you want to ask or see? **Why**?

A: I want to take history of dysphagia. Also, I want to look at the tongue to see evidence of glossitis. Koilonychia with dysphagia and glossitis is suggestive of **Plummer–Vinson** syndrome.

Q: What is **Plummer–Vinson** syndrome? What are the **features**? How to **treat**?

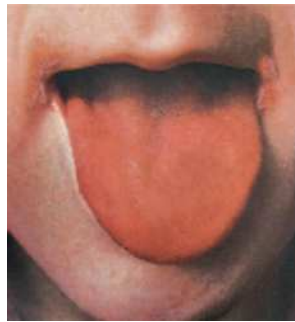
A: It is the combination of:

- Iron deficiency anaemia.
- Dysphagia (due to post-cricoid web secondary to epithelial degeneration).
- Glossitis.

It is also called Paterson–Brown–Kelly syndrome. Common in women, cause is unknown. There is constriction in upper oesophageal sphincter in the post-cricoid region and appears radiologically as a web, which may be asymptomatic or may cause dysphagia. Difficult to see endoscopically. Rarely, there is increased risk of squamous cell carcinoma.



Pallor of palm



Glossitis with angular stomatitis in iron deficiency anaemia



Koilonychia



Koilonychia with leukonychia

Treatment

- If severe anaemia, blood transfusion should be given.
- Iron therapy.
- Rarely, dilatation may be required.

NAIL CHANGES IN DIFFERENT DISEASES

Q: What diseases are diagnosed by examining the nail?

A: Nail abnormality may occur in many local, systemic and dermatological diseases. Hence, these should be examined carefully.

Clubbing and koilonychia: (Already described above).

Leukonychia: It means white nail. It may be diffuse, punctate, linear or striate (white transverse flecks—a normal finding). Causes are:

- May be normal finding in some cases.
- Renal cause (nephrotic syndrome, chronic renal failure).
- Liver diseases (chronic liver disease, cirrhosis of liver).
- Malnutrition (malabsorption, less intake of food).
- Others: Rare (lymphoma, fungal infection, congenital).
- Striate leukonychia (a normal finding due to minor trauma).

Q: What does leukonychia indicate? What is the mechanism of leukonychia? Which organs are involved in leukonychia?

A: It indicates hypoalbuminaemia. However, it may be normal. Mechanism of leukonychia is unknown, it may be due to compression of capillary flow by extracellular fluid. Presence of leukonychia indicates disease of liver, kidney, GIT (malabsorption or less intake of food).

Q: How will you investigate leukonychia?

A: I will take the history of the patient. Investigation should be done according to the history and physical finding. If history is suggestive of CLD or renal disease or GIT disease, I will investigate accordingly.

OTHER DIFFERENT NAIL ABNORMALITIES

Pale nail: It is due to anaemia.

Nail fold infarction: Causes are (usually vasculitis due to any cause)—

- SLE.
- Dermatomyositis.
- Systemic sclerosis.
- Rheumatoid arthritis (RA).
- Polyarteritis nodosa.

Splinter haemorrhage: Causes are:

- Trauma (commonest).
- SBE.
- Septicaemia.
- Collagen disease (vasculitis)—May be due to SLE, RA and polyarteritis nodosa.
- Others: Haematological malignancy, severe anaemia, psoriasis. Rarely in trichinosis (usually transverse haemorrhage).



Leukonychia



Nail fold infarction



Splinter haemorrhage



Half and half nail

Half and half nail: Proximal part of nail is white and distal part is red or brown. Causes are:

- CKD.
- Cirrhosis of liver.
- Occasionally, in normal person.
- Red half moon occurs in congestive cardiac failure.

Nail fold telangiectasia: Causes are:

- SLE.
- Systemic sclerosis.
- Dermatomyositis.
- Mixed connective tissue disease.
- Raynaud's phenomenon.

Beau's line: Non-pigmented transverse line or grooves in nail due to transient arrest of nail growth. Appears at the same time on all nails, a few weeks after an acute illness. Causes are:

- Chronic illness (chronic infection, malignancy and collagen disease).
- Prolonged fever.
- Pneumonia.
- Coronary artery disease.
- Others: Cachexia, malnutrition, psychiatric illness, use of cytotoxic drugs.

Onycholysis: Separation of distal nail plate from the nail bed (free edge looks white). Causes are:

- Psoriasis.
- Fungal infection.
- Thyrotoxicosis (Plummer sign).
- Idiopathic.
- Occasionally drugs (tetracycline and psoralen).
- Porphyria.
- Trauma or faulty manicure.

Green nail: Severe pseudomonas infection.



Nail fold telangiectasia



Beau's line



Yellow nail



Mee's line

Mee's line: Single transverse white band in nail. Causes are:

- Chronic arsenic poisoning.
- CKD.
- Also, after chemotherapy and severe illness.

Yellow nail: Found in yellow nail syndrome, an inherited disease in which the nails are thick, yellow or pigmented with separation of distal part of nail bed due to hypoplasia of lymphatic system. It is associated with lymphoedema of legs, bronchiectasis and pleural effusion.

Nicotine stain: Found in smokers.

Loss of nail (or dystrophy): Causes are:

- Severe lichen planus.
- Epidermolysis bullosa.
- Trauma (tooth biting).

Nail pitting (depression in nail): Causes are:

- Psoriasis.
- Alopecia areata.
- Atopic eczema (when involves proximal nail bed).
- Pityriasis rosacea.



Pitting with onycholysis



Pitting in toe



Pitting in finger

Nail overgrowth: Also called onychogryphosis ('ram's horn nails'), is seen in older people or due to long-term pressure on the nails. It is harmless, sometimes it can be removed.

Brittle nail (easily broken): Causes are:

- Iron deficiency anaemia.
- Peripheral vascular disease.
- Fungal infection.
- Hypocalcaemia.
- Others—Psoriasis, injury (nail biting), idiopathic.



Nicotine stain



Paronychia



Nail biting



Nail overgrowth

Paronychia: It is the inflammation of skin around a finger or toenail. It may be acute or chronic. Also called whitlow.

Nail biting (onychophagia): Common in children. May be found in psychiatric disease or anxiety.

Fungal nail: Nail has thick, white, green, black, discolouration and crust formation.

Absent or small, dysplastic nail: Its causes are:

- Nail patella syndrome (autosomal dominant, associated with no or hypoplastic patella and glomerulonephritis, abnormalities in eye).
- Others: Congenital, traumatic and vasculitis.

Blue nail: Normal white lunula become blue, found in Wilson's disease due to deposition of copper (normally, half-moon lunula at the proximal end of nail is white blue, half moon). Also found in cyanosis and ochronosis, drug therapy (minocyclin, hydroxyurea).

Red nail: May be normal finding. Also in polycythaemia, carbon monoxide poisoning (cherry red).

Brown nail: Usually present in chronic kidney disease (CKD).

Periungual or subungual fibroma: Suggests tuberous sclerosis (epiloia).

Nail hyperpigmentation: May occur due to some drugs (such as zidovudine, doxorubicin, bleomycin, cyclophosphamide, fluorouracil, melphalan and nitrosoureas).



Hypoplastic nail



Onycholysis



Fungal nail



Onycholysis

Terry nail: Proximal part is white or pink, but nail tip is red or brown. It is due to decrease in vascularity and increase in connective tissue within the nail bed. Causes are:

- Old age (normally present in elderly).
- Cirrhosis of liver.
- CCF.
- Hyperthyroidism.
- Malnutrition.
- Renal failure

Dark nail: May be a normal finding, mostly in black people. Sometimes may be due to subungual melanoma.



Blue nail



Periungual fibroma



Dark nail



Terry nail

N.B. Remember the following points:

- Normal nail growth is 0.1 mm/day, finger nails grow quickly than toe nails.
- Nail plate grows continuously and slowly at the rate of 1 cm every 3 months. Hence, renewal of finger nails take about **3 to 6 months**, and toe nails that grow more slowly take 1 year.
- Rapid growth of nail plate occurs in psoriasis.
- Nail growth is arrested by acute illness and ischaemia (Beau's line).

EXAMINATION OF HANDS

Instructions by the examiner:

- Look at the hands. What is the diagnosis? (In a typical case).
- Examine the hands.

By looking, the obvious diagnosis may be:

- Rheumatoid arthritis (to examine rheumatoid hand, see in the Chapter 9).
- Systemic sclerosis (see in the Chapter 9).
- Tophaceous gout.
- Bouchard nodes, Heberden node (in osteoarthritis).
- Skin rash and Gottron patch (dermatomyositis).
- Large size (acromegaly).
- Carpopedal spasm.
- Claw hand.
- Wrist drop.
- Myotonic dystrophy (diagnosed by handshake, then asking the patient to close and open the hands).
- Raynaud's disease or phenomenon.
- Arachnodactyly.
- Syndactyly.
- Polydactyly.
- Short 4th metacarpal.
- Palmar erythema.
- Nail and nail bed change:(Described above)—Clubbing, koilonychia, leukonychia, jaundice, cyanosis, half and half nail, splinter haemorrhage, Beau's line, Mee's line, nail fold telangiectasia and erythema, fungal infection, periungual fibroma, nail pitting, yellow nail syndrome, absent nail, onycholysis, nicotine stain.
- Dupuytren's contracture.
- Trophic change (gangrene, ulceration).
- Wasting (thenar, hypothenar or generalized).
- Tremor.
- Warm and sweaty palm (thyrotoxicosis), cold and sweaty palms (anxiety).
- Single palmar crease (in Down syndrome).



Arachnodactyly



Polydactyly



Short 4th metacarpal
(left hand)



Syndactyly in right index
with middle, polydactyly in left

Q: What **diagnoses** are possible by looking at the fingers?

A: As follows:

- Arachnodactyly—Long, slender fingers. Cause—May be normal, Marfan's syndrome, homocystinuria.
- Syndactyly—United or joined fingers. Cause—Congenital, Poland syndrome.
- Polydactyly—Extra finger. Cause—Congenital, Bardet-Biedl syndrome.
- Clinodactyly—Curved fingers, common in little finger. Cause—Down's syndrome.
- Sclerodactyly—Tapering of fingers due to tightening of skin. Cause—Systemic sclerosis.
- Thick, large, spade like fingers. Cause—Acromegaly.
- Short 4th metacarpal (brachydactyly). Causes are: Down's syndrome, Turner's syndrome, Mucopolysaccharidoses.
- Swann neck, boutonniere, Z deformity of thumb. Cause—Rheumatoid arthritis.

Q: What **diagnoses** can be made by shaking the hands?

A: As follows:

- Warm and sweaty hands—Thyrotoxicosis.
- Cold and sweaty hands—Anxiety.
- Dry and coarse hands—Hypothyroid.
- Doughy feeling—Acromegaly.
- Slow relaxation of grip—Myotonia.
- Rough with thickening of the skin—Arsenicosis, manual worker.



Single palmar crease in
Down's syndrome



Myotonic dystrophy



Myotonic dystrophy



Systemic sclerosis

If you are asked to examine the hands, look as above with a friendly handshake. Then proceed as follows:

If obvious Rheumatoid arthritis or systemic sclerosis or acromegaly, examine accordingly (described in the respective chapters).

If wasting is obvious, see the site—generalized or localized (thenar or hypothenar):

- If there is thenar wasting only: It indicates median nerve lesion.
- If there is hypothenar and other muscles wasting (except thenar): Indicates ulnar nerve lesion.
- On the dorsum: Wasting with dorsal guttering (interossei), indicates ulnar nerve lesion.
- Generalized wasting: Indicates C8 and T1 lesion.

Then, perform the **neurological** examination as follows:

1. Sensory tests in the sensory supply along ulnar and median nerve (if wasting is present, but sensory is intact, more likely diagnosis is motor neuron disease).
2. Next, perform the motor function of hand muscles (ask to the patient as follows):
 - Open and close the hands as quickly as possible (observe weakness and evidence of myotonia dystrophica).
 - Point your thumb towards the ceiling and stop me from bending it (test for abductor pollicis brevis).
 - Fix the tip of little finger and thumb and stop me from separating it (test for opponens pollicis).
 - Spread your fingers wide apart and stop me pushing them together (test for dorsal interossei, **DAB** means dorsal abduction).
 - Hold a piece of paper between two fingers and stop me from taking it out (test for palmar interossei, **PAD** means palmar adduction).
 - Hold a paper between thumb and index finger and stop me from taking it out (test for adductor pollicis). If the muscle is paralyzed, the patient can hold the paper by flexing thumb. It is called **Froment's sign**. It indicates ulnar nerve lesion.
 - Squeeze my fingers (test for C8 and T1 lesion), long and short flexors of the fingers.



Prayer sign



Syndactyly in right index and middle fingers



Wasting of thenar and hypothenar muscles



Ulnar claw hand

Q: What are the findings in hand in infective endocarditis?

A: As follows:

- Osler nodes (small painful violaceous raised nodule, 0.5 to 1.5 cm, present on the tip of the fingers and toes, also palmar aspect, probably due to vasculitis or septic emboli).
- Splinter haemorrhage.
- Clubbing.
- Janeway lesion (large painless erythematous macule containing bacteria on palm, pulp of the fingers. It may be found in the sole).
- Petechial haemorrhage.
- Infarction at the tip of the fingers.



Splinter haemorrhage



Osler node

Dupuytren contracture
with palmar erythema

Clubbing with Beau's line

Q: What are the findings in hand in CLD?

A: As follows:

- Palmar erythema.
- Dupuytren's contracture.
- Clubbing.
- Leukonychia.
- Flapping tremor.
- Cyanosis.
- Spider angioma.
- Pigmentation.
- Jaundice.
- Scratch mark.
- Xanthoma.



Spider angioma

Digital infarction in
peripheral arterial disease

Heberden node



Rheumatoid hand

GENERALIZED OEDEMA

Instruction by the examiner:

- Perform the general examination of the patient
- Look at the patient, what is your finding?

Presentation of a Case:

- This patient has generalized oedema (also called anasarca), involving the whole body, more marked in both legs. Oedema is pitting.

My **differential diagnoses** are (causes of generalized oedema):

- Nephrotic syndrome.
- Hypoproteinaemia due to any cause.
- CKD (in advanced stage).
- Decompensated cirrhosis of liver (advanced stage).
- Congestive heart failure (advanced stage).

Q: How can you **differentiate** oedema of cardiac, renal and liver disease clinically?

A: As follows:

- **Cardiac:** In congestive heart failure, oedema is usually dependent, mostly in the leg, associated with engorged and pulsatile neck veins, enlarged tender liver. Other features of cardiac disease are usually present (e.g., Mitral stenosis or regurgitation).
- **Renal:** In nephrotic syndrome, oedema usually starts from the face or periorbital, then descends, later becomes generalized. Urine shows massive proteinuria. In acute glomerulonephritis, oedema is periorbital, associated with scanty, frothy, smoky urine.
- **Liver disease:** In cirrhosis of liver, there is ascites, in advanced stage there may be generalized oedema. Stigmata of CLD are present.



Generalized oedema



Generalized oedema in nephrotic syndrome

READ THE FOLLOWING TOPICS IN RELATION TO OEDEMA

Q: What is **oedema**? What are the **types**?

A: It is defined as excessive accumulation of fluid in the interstitial space. It may be pitting and non-pitting.

Q: What are the causes of **non-pitting** oedema?

A: As follows:

1. Myxoedema.
2. Chronic lymphatic obstruction or lymphoedema due to any cause (see below).

Q: What are the causes of **pitting** oedema?

A: As follows:

- Congestive cardiac failure (CCF).
- Nephrotic syndrome.
- Hypoproteinaemia due to any cause (protein losing enteropathy or less protein intake).
- Deep venous thrombosis.
- Compression of large veins by tumour or lymph nodes.
- Chronic venous insufficiency (varicose vein).
- Drugs (calcium channel blockers—e.g., nifedipine, amlodipine, some NSAIDs).
- Idiopathic (also called ‘fluid retention syndrome’, common in women).

Q: What are the causes of **periorbital oedema** or **puffiness**?

A: As follows:

- Nephrotic syndrome.
- Acute glomerulonephritis (or AKI).
- Myxoedema.
- Cushing’s syndrome.
- SVC obstruction.
- Angioneurotic oedema.
- Surgical emphysema.
- Orbital cellulitis.
- Malignant exophthalmos (in Graves disease).
- Dermatomyositis.

Q: How will you **investigate** a patient with **generalized oedema**?

A: Investigation should be done according to history, physical finding and suspicion of cause.

- Nephrotic syndrome: Urine for R/E, blood for total protein, 24 hours urinary protein. Other investigations according to suspicion of cause.
- CCF: Chest X-ray, ECG, echocardiogram.
- Cirrhosis of liver: LFT (total protein, A:G ratio, prothrombin time, ultrasonography etc.). Other investigations according to suspicion of cause (e.g., test for hepatitis B, C etc.).
- Hypoproteinaemia: Serum total protein and A:G ratio, other investigation according to the history and suspicion of cause.
- Hypothyroidism: FT₃, FT₄, TSH. Other investigations to find out the cause.

CERVICAL LYMPHADENOPATHY

Instruction by the examiner:

- Perform the general examination of the patient.
- Examine the neck.

Once cervical lymph node is palpable, look at the following points:

- Site (anterior or posterior chain, supraclavicular, submental or submandibular in right or left or both sides).
- Number (single or multiple).
- Size (large LN is abnormal, >1 cm is pathological. Size 2×2 cm may be suggestive of neoplastic lesion).
- Consistency (soft or firm, mixed such as some are firm, some soft, or rubbery or hard).
- Tenderness (suggests acute inflammation).
- Discrete or matted (matted in TB).
- Fixation (to underlying structure or overlying skin suggests malignancy).
- Skin (sinus, ulcer, signs of acute inflammation). Tethering of skin suggests malignancy. Note for scar mark (biopsy), if any.

Presentation of a Case:

- There are cervical lymphadenopathy involving the anterior chain in right or left side (mention the site), which are of variable size and shape, firm in consistency, some are matted, non-tender, free from the underlying structure and overlying skin.
- There is no sinus or scar mark.

Q: What **relevants** do you like to see?

- Lymph nodes in other parts (axillary, inguinal, para-aortic).
- Liver and spleen (found in lymphoma and leukaemia).
- Anaemia and bony tenderness (present in leukaemia).
- Purpura or bruise or petechiae (may be present in leukaemia).
- Palatal petechial haemorrhage (may be present in infectious mononucleosis).
- Cachexia (in disseminated TB or secondaries).



Cervical lymphadenopathy



Cold abscess



Scar mark of LN biopsy



Tuberculous sinus

Q: In which disease, **biopsy** should not be done?

A: Leukaemia (biopsy is not done in leukaemia, rather it is contraindicated. Leukaemia is diagnosed by blood and bone marrow examination. If biopsy is done in leukaemia, there may be uncontrolled bleeding or delay in healing).

FNAC or biopsy of LN in TB shows the following:

- In 50% cases, AFB is positive.
 - In 70 to 80% cases, mycobacterial C/S is positive.
- Granuloma is present in most cases.

Q: What are the **common causes** of cervical lymphadenopathy?

A: As follows:

- Viral—Infectious mononucleosis, CMV infection, HIV.
- Tuberculous lymphadenitis (commonest).
- Infection by atypical mycobacteria.
- Actinomycosis.
- Acute and chronic lymphatic leukaemia.
- Lymphoma.
- Reactive hyperplasia (secondary to infection in mouth or teeth).
- Metastasis (usually supraclavicular).

Q: What are the **causes** of cervical lymphadenopathy in this case?

A: According to the characteristics of the lymph nodes of that patient, mention the common causes as follows:

1. If matted cervical lymphadenopathy with firm in consistency the causes are:

- Tuberculous lymphadenitis (commonest).
- Infection by atypical mycobacteria.
- Actinomycosis.

2. If lymphadenopathy with sinus, the causes are:

- Tuberculous lymphadenitis.
- Actinomycosis.

3. If lymphadenopathy with biopsy marking, the causes are:

- Tuberculosis.
- Lymphoma.
- Secondaries.

4. If hard lymphadenopathy or immobile, fixed to skin or underlying structure, the cause is:

- Metastatic malignancy (e.g., from bronchial carcinoma).

5. If tender cervical lymphadenopathy, the causes are:

- Infection of lymph node itself.
- Acute inflammation secondary to dental sepsis, tonsillitis and mastoiditis.
- May be acute leukaemia.

6. If lymphadenopathy is discrete, soft in consistency, non-tender the causes are:

- Viral—Infectious mononucleosis, CMV infection, HIV.
- Acute and chronic lymphatic leukaemia.
- Lymphoma.
- Reactive hyperplasia.

7. If lymphadenopathy are soft, rubbery and discrete, the cause is:

- Lymphoma.

8. If lymphadenopathy with goitre, the cause is:

- Papillary carcinoma of thyroid with metastasis.

Q: What investigations are done in tuberculous lymphadenitis?

A: As follows:

- CBC and ESR (high).
- Chest X-ray, PA view (to see TB in chest).
- Tuberculin test (MT).
- FNAC or biopsy (FNAC shows granulomatous lymphadenitis, biopsy shows caseation necrosis).

Q: How to treat tuberculous lymphadenitis?

A: With standard anti Koch's usually for 1 year.

N.B.: After anti-TB drug therapy, LNs may be enlarged. It is due to hypersensitivity reaction to tuberculo-protein, released from dead mycobacteria.

Q: What are the atypical mycobacteria?

A: Atypical mycobacteria, also called non-tuberculous mycobacteria (NTM) or mycobacteria other than TB (MOTT), which are:

- Mycobacterium scrofulaceum.
- Mycobacterium avium intracellulare complex (MAC).
- Mycobacterium kansasii.
- Mycobacterium bovis.
- Mycobacterium xenopi.
- Mycobacterium chelonae.
- Mycobacterium malmoense.
- Mycobacterium marinum.
- Mycobacterium fortuitum.

Atypical mycobacteria commonly affect the children. It may also cause disseminated infection in HIV, pulmonary infection (by MAC).

Q: How to treat atypical mycobacteria?

A: If localized involvement in cervical LN, surgical excision. Most organisms are resistant to standard anti-TB drug.

Drugs used are the combination of:

- Clarithromycin 500 mg twice daily or azithromycin 500 mg daily **plus**
- Ethambutol 15 mg/kg **plus**
- Rifabutin 300 mg daily.

However, standard anti-TB therapy with rifampicin, ethambutol, isoniazid (INH) and pyrazinamide are commonly used. Injection streptomycin is also effective. Remember, if no response, there is possibility of MDR-TB.

Causes of localized lymphadenopathy in different sites:

1. Epitrochlear: This is always pathological. Causes are:

- Localized infection in hand or arm (the commonest cause).
- Lymphoma (usually non-Hodgkin's).
- Sarcoidosis.
- Secondary syphilis.
- Tularaemia.

2. Unilateral axillary lymphadenopathy: Causes are:

- Local infection in upper extremity.
- Carcinoma of breast with metastasis.
- Lymphoma (non-Hodgkin commonly).
- Brucellosis.
- Cat-scratch disease.

3. Scalene LNs involvement: Causes are:

- Lymphoma.
- Metastasis from carcinoma of bronchus.
- Sarcoidosis.
- TB.

N.B. Remember the following points

1. If only left supraclavicular LN is palpable, it is called Troisier's sign. Then palpate abdomen to see epigastric mass (carcinoma of stomach).
2. For a particular area of lymphadenopathy, examine the drainage area:
 - Cervical lymphadenopathy (examine the mouth, tonsil, teeth, face, ears and scalp).
 - Axillary lymphadenopathy (examine the breasts, chest and upper limbs).
 - Supraclavicular lymphadenopathy (examine the chest for bronchial carcinoma).
 - Inguinal lymphadenopathy (examine the lower limbs for any septic focus, genitalia and perineum).

GENERALIZED LYMPHADENOPATHY

Instruction by the examiner:

- Perform the general examination of this patient.

Presentation of a Case:

- This patient has generalized lymphadenopathy involving cervical, supraclavicular, axillary and inguinal lymph nodes which are of variable size and shape, some are firm and some are rubbery in consistency, discrete, non-tender and free from underlying structure and overlying skin.

Q: What **relevants** do you like to see?

A: As follows:

- Liver and spleen (lymphoma and leukaemia).
- Anaemia and bony tenderness (leukaemia).
- Purpura or bruise or petechiae (leukaemia).
- Palatal petechial haemorrhage (infectious mononucleosis).
- Cachexia (disseminated TB or secondaries).

Q: What are the **causes** of generalized lymphadenopathy in this case?

A: (Mention the common causes of that patient, considering the age):

If the patient is young or child, the causes are:

- Lymphoma (usually Hodgkin's disease).
- Acute lymphoblastic leukaemia.
- Viral infection (infectious mononucleosis and cytomegalovirus infection).
- Others: Disseminated TB, SLE.

If the patient is middle aged or elderly, the causes are:

- Lymphoma.
- Chronic lymphatic leukaemia.
- Viral infection (infectious mononucleosis and cytomegalovirus infection).
- Others: Sarcoidosis, brucellosis, toxoplasmosis and HIV.
- Disseminated TB.

READ THE FOLLOWING TOPICS IN RELATION TO GENERALIZED LYMPHADENOPATHY

Q: What are the **causes** of generalized lymphadenopathy? (theoretically).

A: As follows:

- Viral infection: Infectious mononucleosis, CMV, HIV.
- Bacterial: Brucellosis, Septicaemia, Disseminated tuberculosis, Cat scratch disease.
- Haematological malignancy: Acute and chronic lymphoblastic leukaemia, Lymphoma, CML (in blast crisis).
- Collagen vascular disease: SLE, RA.
- Drugs: Phenytoin or diphenylhydantoin (called pseudolymphoma).
- Others: Sarcoidosis, toxoplasmosis, secondary syphilis.

Q: If the patient has **generalized lymphadenopathy with arthritis**, what are the likely causes?

A: As follows:

- Juvenile idiopathic arthritis (Still's disease).
- SLE.
- Felty's syndrome.
- Sarcoidosis.
- Viral—infectious mononucleosis, CMV infection.
- Brucellosis.

Q: What are the **causes** of lymphadenopathy with splenomegaly (and/or hepatomegaly)?

A: As follows:

- Lymphoma.
- ALL or CLL.
- Infectious mononucleosis.
- SLE.
- Felty's syndrome.
- Sarcoidosis, brucellosis and toxoplasmosis.
- Disseminated tuberculosis.
- HIV.

Q: What are the causes of **generalized lymphadenopathy** with fever?

A: As follows:

- Viral infections (e.g., infectious mononucleosis, CMV infection).
- Lymphoma.
- ALL and CLL.
- Disseminated tuberculosis.
- Brucellosis.
- Sarcoidosis.
- Toxoplasmosis.

Q: If a patient **presents** with generalized lymphadenopathy, how will you **proceed** to diagnose?

A: History of the patient (such as fever, loss of weight, sweating, itching), physical examination (lymphadenopathy, hepato-splenomegaly, skin rash, joints) and investigations.

Q: What **investigations** do you suggest in generalized lymphadenopathy?

A: As follows:

- CBC, ESR, PBF (to exclude leukaemia, high eosinophil in Hodgkin's lymphoma, atypical lymphocyte in infectious mononucleosis, high ESR in TB).
- Chest X-ray (to see TB, bilateral hilar lymphadenopathy in lymphoma and lymphatic leukaemia).
- Ultrasonography or CT scan of abdomen (to see hepatomegaly, splenomegaly, para-aortic lymphadenopathy).
- Others according to the suspicion of cause:
- If lymphoma is suspected: FNAC or biopsy (biopsy is preferable) of lymph nodes.
- If leukaemia is suspected: Bone marrow study.
- If disseminated tuberculosis: MT, FNAC or biopsy.
- If HIV is suspected: HIV screening test.
- If SLE: ANA, anti-ds-DNA.

N.B. Remember the following points:

- *Normal LNs may be palpable in axilla, groin, usually up to 0.5 cm, which are soft, rubbery, shotty. Submandibular LNs <1 cm is normal in children and inguinal LNs <2 cm is normal in adult.*
- *Reactive LNs expand rapidly and may be painful.*
- *Localized lymphadenopathy means single anatomical area of LN involvement.*
- *Generalized lymphadenopathy means 3 or more anatomical non-contiguous areas of LN involvement.*
- *Enlargement of supraclavicular and scalene LNs are always pathological.*

Lymphoreticular System: Includes lymph nodes, spleen, tonsil, adenoid, Peyer's patch of ileum, Waldeyer's ring and Kupffer cells in liver.

PIGMENTATION

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the patient. What is your finding? (Pigmentation may be found). Examine the relevant.

Once there is pigmentation, look carefully at the following points:

- Is it generalized or localized to a part?
- Look at the—
 - Lips, gum, inner side of mouth or buccal mucosa and tongue.
 - Exposed parts (face, neck and extensors of arm).
 - Palm (especially the creases).
 - Pressure areas (knee or elbow).
 - Scars (especially recent).
 - Nipples.
 - Genitalia.

Presentation of a Case:

- There is generalized pigmentation involving the whole body, gums, buccal mucosa and tongue (or mention the site, if localized). Vitiligo is present (mention if any).

Q: What do you think are the **causes** in this case?

A: **Mention** the causes of that patient:

- Kala-azar (history of fever).
- Addison's disease.
- Haemochromatosis.
- Primary biliary cirrhosis (especially in middle aged or elderly female).
- Drugs (e.g., busulphan, amiodarone, phenothiazine).
- Chronic debilitating illness (malignancy, CKD, TB).
- Chronic arsenic toxicity.
- Malabsorption syndrome (e.g., Whipple's disease).

Q: What **history** and relevant **physical finding** do you want to see in a patient with pigmentation?

A: As follows:

1. History of fever (e.g., kala-azar).
2. History of drugs.
3. History suggestive of chronic liver disease (CLD), primary biliary cirrhosis (itching may be present), chronic kidney disease (CKD), Addison's disease (Low BP, weakness).
4. Physical examinations:
 - BP low and patient looks emaciated (in Addison's disease).
 - Hepatosplenomegaly (in kala-azar).
 - Signs of CLD or haemochromatosis or PBC (For details, see in the respective chapters).
 - Abdomen (scar of bilateral adrenalectomy in Nelson's syndrome).
 - Evidence of other chronic illness.



Haemochromatosis



Systemic sclerosis



Generalized pigmentation



Addison's disease

Q: What are the **causes** of localized pigmentation?

A: Any cause of generalized pigmentation may be manifested as localized pigmentation initially. Other causes are:

- Local radiation therapy, friction or scratching.
- Melasma.
- Erythema ab igne (see in respective topic).



Skin crease pigmentation

Perioral pigmentation in
Peutz-Jeghers syndromeOchronosis
(ear pigmentation)

Q: What is **Peutz-Jeghers syndrome**?

A: It is a disorder inherited as autosomal dominant, characterized by mucocutaneous pigmentation of lips, around the mouth, eyes, nose, buccal mucosa (never tongue), hands and feet, associated with polyp in GIT. Polyp is usually hamartomatous, benign, involves any part of GIT, commonly small bowel. It may cause bleeding, recurrent abdominal pain, intestinal obstruction and intussusception. Rarely it turns to malignancy.

Treatment:

- Polypectomy. Laparoscopic-assisted enteroscopy may be helpful for polyp removal.
- Small bowel resection is usually avoided (polyp may recur). However, laparotomy and resection may be necessary, for small intestinal intussusception, obstruction or persistent intestinal bleeding.



Vitiligo



Albinism



Pityriasis versicolor



Leprosy (Lepros reaction)

Q: What are the causes of hypopigmentation?

A: Causes of hypopigmentation:

1. **Generalized:** Albinism, Panhypopituitarism.

2. **Localized:**

- Vitiligo.
- Post burn.
- Leprosy (Tuberculoid).
- Pityriasis versicolor.
- Pityriasis alba (depigmented areas on the face, common in children).
- Idiopathic guttate hypomelanosis (multiple small areas of depigmentation in chronically sun exposed skin).
- Phenylketonuria.

Q: What are the causes of hyperpigmentation?

A: Causes of pigmentation: It may be physiological and pathological—

A. Physiological: familial, racial, pregnancy, prolonged exposure to sun.

B. Pathological:

1. Endocrine causes:

- Addison's disease (brown or dark brown).
- Cushing's syndrome.
- Acromegaly.
- Nelson's syndrome (after bilateral adrenalectomy).
- Thyrotoxicosis.
- Ectopic ACTH syndrome.

2. Infections: kala-azar.

3. Chronic liver disease:

- Haemochromatosis (greenish or bronze, less involvement of mucous membrane).
- Cirrhosis of liver (common in PBC).

4. GIT: Malabsorption syndrome (Whipple's disease, Peutz-Jeghers syndrome).

5. Chronic debilitating illness:

- Internal malignancy (commonly ectopic ACTH syndrome), CKD, any chronic illness.

6. Drugs:

- Cytotoxic drugs e.g., busulphan (diffuse brown), bleomycin (diffuse brown, often in flexural parts), any cytotoxic drug.
- Amiodarone (violaceous or brown or blue or slaty-grey, in exposed parts).
- Phenothiazine (slaty-grey, exposed site).
- Phenytoin (melasma-like pigmentation).
- Oral contraceptive pill.
- Chloroquine (blue-grey, in exposed parts).
- Clofazimine (red or pinkish).
- Psoralen (brown, exposed site).
- Minocycline (Slaty-grey, scars, temples, shins and sclera).
- Mepacrine (yellow).

7. Others:

- Chronic arsenic poisoning.
- Pellagra (necklace area and exposed part).
- Systemic sclerosis.
- Ochronosis (mainly in the joint, nose, ear and face).
- Argyria (slaty grey hue due to silver deposition).
- Porphyria cutanea tarda.
- Acanthosis nigricans.
- Melanoma

Q: Why **drug** causes pigmentation?

A: This is due to melanocyte stimulation or deposition of drug in the skin.

Q: How to **investigate** in a patient with pigmentation?

A: According to the history and suspicion of causes (kala-azar, Addison's disease, haemochromatosis).

ERYTHEMA AB IGNE

Instruction by the examiner:

- Perform the general examination of the patient.
- Look here. What is the diagnosis?

Presentation of a Case:

- There is reticular pattern of pigmentation involving (mention the location e.g., thigh, abdomen, shoulder).

Diagnosis is erythema ab igne.

Q: What is the underlying **disease**? What **history** do you like to take?

A: Hypothyroidism or severe pain. There may be history of application of hot water bag or bottle to relieve pain or to relieve from cold.



Erythema ab igne (legs)



Erythema ab igne (arm)



Erythema ab igne (abdomen)

Q: What is **erythema ab igne**?

A: It is characterized by reticular pattern of pigmentation that occurs due to prolonged exposure to excessive heat without production of burn. It is due to repeated infrared heat injury. Occurs at any part of the body, where heat is applied. Histology shows increased amount of elastic tissue in dermis.

Q: What are the **causes** of erythema ab igne?

A: As follows:

- Those who sit near the fire or those who use hot water bottle on belly or thigh or on back due to severe pain.
- Hypothyroidism (patient applies hot because of coldness).

Q: How to treat?**A:** As follows:

- 0.1% retinoic acid with 0.1% dexamethasone cream applied locally or 5% hydroquinone applied locally.
- Treatment of underlying cause (e.g., hypothyroidism).

Q: What are the **complications** of erythema ab igne?**A:** In long-standing cases, premalignant keratosis and squamous cell carcinoma.**Q:** What are the **differential diagnoses** of reticular pattern of pigmentation?**A:** As follows:

- Erythema ab igne.
- Livedo reticularis.
- Cutis marmorata (a physiological reaction to cold in children and adult).

GYNAECOMASTIA

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the chest. What is your finding? What else do you want to examine?

Proceed as follows:

- Look at the chest (unilateral or bilateral breast enlargement).
- Palpate the glandular tissue, first with palm, then with fingers (to differentiate from *lipomastia in obese*).
- Tender or non-tender.
- Any secretion.

Presentation of a Case:

- There is right or left or bilateral gynaecomastia, tender (or non-tender). Right or left is larger.

Q: What else or relevants do you want to examine to find out causes?

A: As follows:

- Age (in young, puberty gynaecomastia).
- History of taking drugs (spironolactone, digoxin, oestrogen).
- Stigmata of chronic liver disease.
- Chest—To see evidence of bronchial carcinoma (in elderly with cachexia, clubbing with nicotine staining, radiation mark in chest).
- Body habitus (tall and obese, small testes, absent or less secondary sex characters in Klinefelter's syndrome).
- Palpate the testes (to see atrophy, tumour or ambiguous genitalia).
- Endocrine abnormality (hypopituitarism, thyrotoxicosis, Addison's disease).

Q: What do you think the causes in this patient?

A: Mention the causes according to age of the patient:

If the patient is young, the causes are:

- Puberty (normal physiological).
- Drugs (spironolactone, digoxin, INH).
- Testicular tumour (teratoma and Leydig cell tumour).
- Secondary testicular failure (trauma, orchidectomy, leprosy).
- Chronic liver disease (due to Wilson's disease, alpha-1-antitrypsin deficiency).

If the patient is elderly or middle aged, the causes are:

- Drugs (as above, also oestrogen therapy for carcinoma of prostate).
- Chronic liver disease.
- Bronchial carcinoma.
- Testicular tumour.
- Secondary testicular failure (trauma, orchidectomy, leprosy).

Q: How to **differentiate** gynaecomastia from lipomastia?

A: As follows:

- Lipomastia is due to deposition of fat in the breast. It is soft.
- Gynaecomastia is the enlargement of male breast due to glandular tissue proliferation. It is firm, hard or rubbery.

N.B. Remember the following points:

- Unilateral gynaecomastia in the elderly is highly suspicious of malignancy (which is hard, fixed to underlying tissue, associated with skin tethering and nipple discharge).
- In male, carcinoma of breast is 16 times common in Klinefelter's syndrome.



Bilateral gynaecomastia



Lipomastia with striae in Cushing's syndrome



Lipomastia



Gynaecomastia (Klinefelter's)

READ THE FOLLOWING TOPICS IN RELATION TO GYNAECOMASTIA

Q: What is **gynaecomastia**?

A: Enlargement of male breast due to proliferation of glandular components. It is due to alteration of normal ratio of active androgen to oestrogen in plasma or breast (normal ratio of testosterone:oestrogen in breast is 100:1 and in blood is 300:1). Imbalance occurs either due to less testosterone production or action or increased oestrogen synthesis or both.

Q: What are the **causes of gynaecomastia**?

A: It may be physiological or pathological.

A. Physiological:

1. Puberty (50% cases), may be unilateral due to transient increase in oestradiol level. Resolves spontaneously in 6 to 18 months.
2. Senile (40% or more) due to increased oestrogen from conversion of androgen to oestrogen (also decline of Leydig cell in testis).
3. Newborn (due to transplacental transfer of maternal oestrogen).

B. Pathological:

1. Chronic liver disease (common in alcoholic liver disease), hepatocellular carcinoma (hcg secreting).
2. Bronchial carcinoma (5% case, hcg secreting).

3. Hypogonadism:

- Primary testicular diseases—which may be due to testicular tumour, teratoma, Leydig cell tumour, trauma, orchidectomy, radiation, leprosy, TB, mumps orchitis, haemochromatosis, Klinefelter's syndrome.
 - Secondary testicular failure (hypopituitarism, hyperprolactinaemia, Kallmann syndrome).
4. Endocrine disease (e.g., acromegaly, thyrotoxicosis, hypothyroidism, adrenal carcinoma, Addison's disease).
5. Drugs (spironolactone, digoxin, INH, oestrogen therapy for prostate carcinoma, alcohol, alkylating agent, methyldopa, marijuana, amiodarone).
6. Chromosomal abnormalities: (e.g., Klinefelter's syndrome, Kallmann syndrome).
7. Others: Testicular feminization syndrome, starvation and idiopathic.

Q: What are the causes of painful gynaecomastia?

A: As follows:

- Puberty.
- Drugs (spironolactone).
- Chronic liver disease.

Q: What is Kallmann syndrome?

A: Kallmann syndrome is a form of hypogonadotropic hypogonadism, due to a failure of the hypothalamus to release gonadotrophin releasing hormone (GnRH), characterized by anosmia, cryptorchidism, small testis, cleft lip or palate. There is low luteinizing hormone (LH), follicle stimulating hormone (FSH) and low testosterone. At puberty, affected individuals do not develop secondary sex characteristics, such as the growth of facial hair and deepening of the voice in males. Affected females usually do not begin menstruating at puberty and have little or no breast development. In some people, puberty is incomplete or delayed.

Q: What are the mechanisms of gynaecomastia?

A: 4 possible mechanisms are:

1. Increased oestrogen, causes are—CLD, bronchial carcinoma, Leydig cell tumour of the testis, adrenal carcinoma and congenital adrenal hyperplasia, thyrotoxicosis.
2. Reduction of circulating androgens, causes are—Klinefelter's syndrome, primary and secondary hypogonadism, testicular failure.
3. Antagonism of androgen action (using spironolactone).
4. Androgen resistant state or insufficiency (in testicular feminization syndrome).

Q: Why gynaecomastia in CLD?

A: Excess oestrogen due to altered metabolism by liver and spironolactone therapy for ascites.

Q: Why alcohol causes gynaecomastia?

A: By causing CLD or by damaging Leydig cells of testis without CLD.

Q: How will you investigate a case of gynaecomastia?

A: Depends on cause—

- If the patient is young, it may be due to puberty. No need of further investigation.
- If due to drug, no need of further investigation.

Otherwise investigations are:

1. Chest X-ray (to exclude bronchial carcinoma).
2. Liver function tests (in CLD).
3. Endocrine evaluation:
 - In hypogonadism—serum testosterone, LH, FSH, oestradiol, prolactin and hcg. (If LH and FSH are high, but testosterone is low, likely cause is primary testicular failure. If both LH and testosterone are low, likely cause is increased oestrogen from tumour of testis. If both LH and testosterone are high, likely cause is androgen-resistant state or gonadotrophin-secreting tumour. If plasma β -hcg is increased, likely cause is testicular tumour).
 - 24 h urinary 17-ketosteroid or serum and androstenedione should be done (congenital adrenal hyperplasia).
4. Other investigations: Chromosomal analysis in Klinefelter's syndrome.

Q: How will you treat gynaecomastia?

A: As follows:

- Explanation and reassurance to the patient. If due to puberty, disappears spontaneously.
- Treatment of primary cause. Offending drug should be stopped.
- If severe and progressive or suspicion of malignancy, mastectomy should be done.

ERYTHEMA NODOSUM

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the leg. What is your finding? What else do you want to examine?

Look carefully the following points (look and feel):

- Swelling (multiple, nodular, variable in size and shape).
- Colour (red-to-bluish or pigmented).
- Palpate (Tender nodule: Look at the face, patient winces, if pain).

Presentation of a Case:

- There are multiple nodular, tender lesions of variable size and shape, some are red and some are pigmented in the anterior surface of right or left or both shins.

Q: What are the **possibilities**?

A: My differential diagnoses are:

- Drug rash.
- Erythema nodosum.
- Erythema multiforme.
- Purpura.
- Erythema induratum.
- Others: Nodular panniculitis, meningococcal septicaemia, vasculitis (SLE, polyarteritis nodosa).

Q: What is the **most likely** diagnosis?

A: Erythema nodosum.

READ THE FOLLOWING TOPICS IN RELATION TO ERYTHEMA NODOSUM

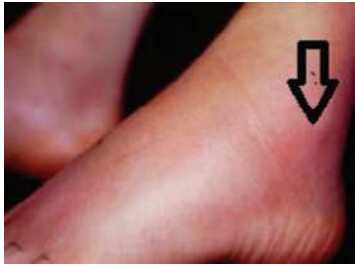
Q: What is **erythema nodosum**? What are the **histological** findings?

A: It is characterized by non-suppurative, painful, palpable, erythematous nodular lesion in the skin due to delayed hypersensitivity reaction in dermis and subcutaneous fat. Usually, it is associated with fever and arthralgia, common in shin below the knee. Nodules may be 2 to 6 cm in diameter, occur in crops over 2 weeks, then resolve slowly over months, leaving bruise stain in the skin. It never ulcerates, may be recurrent, common in adult female.

Microscopy: Panniculitis (inflammatory reaction in fat), infiltration of lymphocytes, histiocytes, multinucleated giant cells and eosinophils, immune-complex deposition in dermal vessels. Hallmark is Miescher's granuloma.



Multiple Erythema Nodosum (Leg)



Single Erythema Nodosum (Foot)



Erythema Nodosum (Shin)

Q: In erythema nodosum, what **history and relevants** should be seen?

A: As follows:

1. History:

- Drugs (see below).
- Fever.
- Sore throat or tonsillitis (streptococcal tonsillitis).
- Other infection (TB, leprosy, histoplasmosis).
- Arthritis or arthralgia or other features of sarcoidosis.
- GIT symptoms—diarrhoea, dysentery, pain abdomen (due to inflammatory bowel disease).

2. Examination:

- Throat (tonsillitis).
- LN (sarcoidosis, TB, lymphoma and fungal infection).
- Liver, spleen (sarcoidosis and lymphoma).
- Skin changes (lupus pernio in sarcoidosis, anaesthetic patch or erythematous or nodular lesion in leprosy).
- Ulceration in mouth, genitalia (Behçet's syndrome).
- Evidences of rheumatic fever.

Q: What are the **causes** of erythema nodosum?

A: As follows:

- Sarcoidosis (usually in acute).
- Streptococcus beta-haemolyticus infection (throat).
- Primary pulmonary TB.
- Drugs (sulphonamide, penicillin, oestrogen-containing oral contraceptive pill, salicylates, barbiturates, sulphonylureas, iodides).
- Inflammatory bowel disease (Crohn's disease, ulcerative colitis).
- Fungal infections (histoplasmosis, coccidioidomycosis, common in the USA).
- Protozoal (toxoplasmosis).
- Leprosy (erythema nodosum leprosum).
- Idiopathic (up to 50% cases).
- Others: Brucellosis, rickettsial, mycoplasma and viral infection, pregnancy, lymphoma, cat-scratch disease, Behçet's syndrome, SLE.

Q: What investigations are done in erythema nodosum?**A:** As follows:

- CBC, ESR, PBF (leucocytosis in streptococcal infection, high ESR in TB).
- ASO titre, throat swab for C/S, blood for C/S (in streptococcal infection).
- Chest X-ray (TB and sarcoidosis).
- MT and sputum for AFB (in case of TB).
- LN biopsy (sarcoidosis, lymphoma and TB).
- Inflammatory bowel disease (barium enema double-contrast, sigmoidoscopy or colonoscopy, barium follow through).
- Other investigations: According to suspicion of cause.

Q: How to treat erythema nodosum?**A:** As follows:

1. Treatment of primary cause (e.g., penicillin, if streptococcal infection). It is self-limiting, may resolve in 3 to 6 weeks.
2. Other treatment:
 - Rest.
 - NSAIDs (indomethacin).
 - In severe cases, corticosteroid should be given.
 - Empirically, a short course of potassium iodide 400 to 900 mg daily may be helpful.

Erythema induratum (Bazin's disease): Erythema induratum of Bazin type is a nodular vasculitis, related to tuberculous origin. It is one of the sequelae of immunologic reactions against antigenic components of *M. tuberculosis*, which spreads through blood. Usually due to delayed hypersensitivity reaction to tubercle bacillus. Hepatitis C virus may be a cause. More common in women, 20 to 30 years, in lower extremities, usually in calf muscle, also in shins. Confuses with chilblain, erythema nodosum, erythema nodosum leprosum, pancreatic panniculitis, lupus panniculitis. CBC, ESR, PCR and biopsy should be done. Persistent ulceration may be present. Treated with antituberculous therapy. Steroid may be given. Potassium iodide for local application. If treated properly, the prognosis is good.

Differences between erythema nodosum and erythema induratum:

Points	Erythema Nodosum		Erythema Induratum
1.	Duration	Short	Long
2.	Site	Shin	Calf
3.	Occurrence	Lesions occur simultaneously	Lesions occur serially in crops
4.	Ulceration	Absent	Present
5.	Pain	More	Less
6.	Scarring	Absent	Present
7.	Cause	Multiple causes	Usually TB
8.	Histology	Septal panniculitis	Lobular panniculitis



Erythema induratum



Erythema induratum

LEPROSY (HANSEN'S DISEASE)

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the face, what are your findings?

Presentation of Case 1 (Face):

- There are multiple nodules of variable size and shape involving right or left or both ear lobules, also face and nose.
- Skin of the face is thick, corrugated.
- Loss of lateral one third of eyebrows (If present, mention these).
- There is also saddle deformity of nose, perforation of nasal septum.

Q: What is the likely **diagnosis**?

A: Lepromatous leprosy.



Depressed nasal bridge



Nodules



Hypopigmented patch in chest



Hypopigmented patch and nodule on the back

Q: What are the **possibilities**?

A: My **differential diagnoses** are:

- Post-kala-azar dermal leishmaniasis (PKDL).
- Lepromatous leprosy.
- Sarcoidosis.
- SLE.
- Acne rosacea.
- Dermatomyositis.
- Lupus vulgaris.

Presentation of Case 2 (Hypopigmented Patch):

- There are multiple hypopigmented patches of variable size and shape in the trunk, upper abdomen and back with loss or impairment of sensation over the lesion.

Q: What is the likely **diagnosis**?

A: Tuberculoid leprosy.

Presentation of Case 3 (Multiple Nodules):

- There are multiple nodules on the dorsum of the hand, forearm or leg and foot, which are of variable size and shape. Some of the nodules are painful.

My diagnosis is **erythema nodosum leprosum (ENL)**.



Thickened great auricular nerve and facial lesion



Nodule in dorsum of hand and foot



Erythema nodosum leprosum



Nodule in ear lobule

Q: What are the differential diagnoses of **hypopigmented lesion**?

A: As follows:

- Fungal infection (*Taenia corporis*).
- Tinea versicolor.
- PKDL (early stage).
- SLE.
- Tuberculoid leprosy.
- Psoriasis.

Q: What **investigations** are done to diagnose leprosy?

A: Slit skin smear, nasal scraping or biopsy from skin lesion or thickened nerve for AFB staining. Also skin biopsy should be done for histopathology.

- In tuberculoid type—epithelioid granuloma may be found.
- In lepromatous leprosy—*Mycobacterium leprae* may be found in skin macrophage (also Schwann cells and perineurium).

Q: What **else** do you like to see? Or what are the **nerves** commonly involved in Leprosy?

A: I want to see for nerve thickening. Nerves involved in leprosy are:

1. Supraorbital.
2. Facial (in crossing of zygomatic arch).
3. Great auricular (in posterior triangle in neck).
4. Radial (in humerus).
5. Ulnar (in elbow).
6. Radial cutaneous nerve (in wrist).
7. Median (in wrist).
8. Common peroneal (in back of knee).
9. Posterior tibial and sural (at ankle).

READ THE FOLLOWING TOPICS IN RELATION TO LEPROSY

Q: What is leprosy? What are the types of leprosy?

A: It is a chronic granulomatous disabling disease, caused by *Mycobacterium leprae*. It involves the peripheral nerves, skin, mucous membrane, bone and viscera. Incubation period is 3 to 5 years (Longest incubation period).

Leprosy is divided into 5 types:

1. Tuberculoid leprosy (TT).
2. Borderline tuberculoid (BT).
3. Borderline leprosy (BB).
4. Borderline lepromatous leprosy (BL).
5. Lepromatous leprosy (LL).

Depending on cell mediated immunity, it is of **2 types**:

1. Polar form.
2. Borderline form.

Also, depending on number of organism, it is of **2 types**:

1. Paucibacillary: Skin smear for *Mycobacterium leprae* bacilli is negative or few (found in TT and BT).
2. Multibacillary: Skin smear for *Mycobacterium leprae* bacilli is positive (found in BT, all BB, BL and LL).

Q: What are the complications of Leprosy?

A: As follows:

1. Deformity—Claw hand, foot drop, wrist drop.
2. Blindness due to keratitis, iritis.
3. Orchitis causing primary gonadal failure.
4. Secondary amyloidosis.
5. Peripheral neuropathy.

Q: How to treat leprosy?

A: Treatment depends on type:

1. Paucibacillary (3 to 5 skin lesions, skin smear negative or few, TT and BT):
 - Rifampicin 600 mg monthly (supervised) plus dapsone 100 mg daily (self-administered) for 6 months.
2. Paucibacillary single lesion:
 - Rifampicin 600 mg **plus** Ofloxacin 400 mg **plus** Minocycline 100 mg, in single dose (ROM therapy).
3. Multibacillary (>5 skin lesions, skin smear positive, BT, all BB, BL and LL):
 - Rifampicin 600 mg and clofazimine 300 mg monthly (supervised) **plus** dapsone 100 mg and clofazimine 50 mg daily (self-administered) for 12 months or until smear negative (may be up to 24 months).

Q: What are the **side effects** of dapsone and clofazimine?

A: As follows:

- Dapsone—Haemolytic anaemia, agranulocytosis, exfoliative dermatitis, hepatitis, hypoprotein-aemia, psychosis.
- Clofazimine—Red discoloration of skin, urine and body secretions, anorexia, nausea, vomiting, abdominal pain, pruritus.

Q: What is **lepra reaction**?

A: It is defined as ‘episodes of inflammation in the pre-existing lesion of leprosy’. It may be the first manifestation of the disease. Lepra reaction may be insidious or rapid, destroying the affected tissue within hours. It is of 2 types: Type 1 and type 2.

A. Type 1 is due to delayed hypersensitivity reaction (Type IV), occurs in 30% borderline patients. It occurs spontaneously or precipitated by treatment. There is rapid swelling of one or more nerves with pain and tenderness. Nerve function is lost rapidly. Foot drop, claw hand and facial palsy may occur. Skin lesions become erythematous, swollen and new lesions may appear. There may be oedema of hands, feet and face. Improves after starting treatment and also after completion of drug therapy.

Treatment:

1. In mild case—aspirin 600 mg, 6 hourly.
2. In severe case—prednisolone 40 to 60 mg daily; reduce the dose to 5 mg/day each month, tapered over 3 to 6 months.
3. Clofazimine can be added 300 mg daily. If fails, Cyclosporine 5 to 10 mg/kg may be given.
4. Treatment of leprosy should be continued.

B. Type 2 (also called Erythema Nodosum Leprosum) is due to immune complex deposition (**type III** hypersensitivity reaction), occurs in BL and LL patient who produce antibodies and have a high antigen load.

It is characterized by fever, arthralgia and crops of small pink painful nodules on the face and limbs. Iritis, iridocyclitis, keratitis, conjunctivitis and episcleritis are common.

Other features are neuritis, orchitis, myositis, nephritis, epistaxis, pleurisy, bone pain, arthritis, lymphadenitis and hepatomegaly. ENL may be the first manifestation of leprosy, 50% in lepromatous and 25% in BL, either during the course of the disease or commonly in the second year of treatment. ENL may continue intermittently for several years.

Treatment:

1. In mild cases—aspirin 600 mg, 6 hourly.
2. In severe cases—
 - Thalidomide (100 mg, 6 hourly). When symptoms improve, reduce the dose slowly over weeks or months, maintenance dose is 50 to 100 mg daily. It is a potent teratogenic drug (avoid during pregnancy).
 - If thalidomide is not available, prednisolone (40 to 60 mg) should be given, reduce the dose over 1 to 6 months.
3. Clofazimine—dose is increased.
4. Antileprosy therapy must be continued.

SUPERIOR VENA CAVAL OBSTRUCTION (SUPERIOR VENA CAVAL SYNDROME)

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the patient. What are your findings? What else do you want to examine?(Patient may be dyspnoeic or may have stridor).

See the following points (if asked to look at the patient):

1. Face (oedematous or puffy, red, plethoric, suffused and cyanosed).
2. Eyes:
 - Periorbital oedema.
 - Red eyes, congested conjunctiva (bloodshot eyes).
 - Chemosis (conjunctival oedema).
3. Neck: Swollen, neck veins are engorged and non-pulsatile (in CCF, engorged and pulsatile).
4. Visible tortuous and dilated veins in chest wall and abdomen (see the flow, which is downwards).
5. Upper limb may be oedematous with prominent engorged veins.



Engorged veins in chest



Puffy face with congested eyes



Engorged veins in abdomen



Engorged & non pulsatile neck veins

Presentation of a Case:

- The face is puffy, plethoric and cyanosed.
- There is periorbital oedema, eyes are congested with chemosis.
- The neck veins are engorged and non-pulsatile.
- There are also engorged veins in chest wall and abdomen and the flow is downwards.
- Both the arms are oedematous, clubbing with nicotine staining.
- Under surface of tongue shows multiple venous angiomata.
- There may be radiation mark on the chest wall (mention, if any).

My diagnosis is **SVC obstruction**.

Q: What are the likely **causes** of this patient?

A: Mention the causes according to the age:

- In the elderly or middle aged—Bronchial carcinoma and lymphoma.
- In young or early age—Lymphoma.

Q: Tell **one investigation** that will help the diagnosis of SVC obstruction.

A: Chest X-ray (bronchial carcinoma and lymphoma).

Q: Tell **another investigation**.

A: CT scan of chest.

Q: What **relevant** do you like to examine in this patient to find out cause?

A: As follows:

- Chest (bronchial carcinoma usually Pancoast tumour).
- LNs (lymphoma and metastasis).
- Liver and spleen (lymphoma).
- Clubbing, nicotine stain (bronchial carcinoma).
- Thyroid (to see retrosternal thyroid).
- Signs of Horner's syndrome (in Pancoast' tumour).
- Ophthalmoscopy (dilated vessels, haemorrhage, exudate, rarely papilloedema).

READ THE FOLLOWING TOPICS IN RELATION TO SVC OBSTRUCTION

Q: What are the **causes** of SVC obstruction?

A: As follows:

1. Bronchial carcinoma (commonest, in 75%).
2. Lymphoma (early age, also in the elderly, in 20%).
3. Other causes:
 - Any tumour in mediastinum (e.g., thymoma, germ cell tumour, metastasis to mediastinum).
 - Retrosternal goitre.
 - Chronic fibrotic mediastinitis (which may be idiopathic or secondary to tuberculosis, histoplasmosis, pyogenic infection, radiotherapy).
 - Giant aneurysm of the aortic arch.
 - Carcinoma of oesophagus.
 - Rarely thrombosis, invasion by malignancy and chronic constrictive pericarditis.

N.B. Remember the following points:

- SVC obstruction of recent onset is likely to be due to malignancy.
- SVC obstruction of long-standing is due to non-malignant origin.

Q: What are the **presentations** of SVC obstruction?

A: The patient may present with (or symptoms may be):

1. Breathlessness, cough.
2. Flushing, red, puffy and oedematous face.
3. Headache (early morning), which is severe with coughing. May be syncope, dizziness or blackout, stupor, seizure (due to increased intracranial pressure).

4. Symptoms are aggravated on lying down or bending forward (indicates mediastinal involvement).
5. Other features are due to involvement of neighbouring structures, such as—
 - Stridor (tracheal compression).
 - Hoarseness of voice (recurrent laryngeal nerve involvement).
 - Horner's syndrome (cervical sympathetic chain involvement).
 - Dysphagia (oesophageal compression).

Q: What are the **causes of death in SVC obstruction?**

A: Death is due to:

- Respiratory obstruction.
- Intracranial haemorrhage.

Q: What **investigations are done in SVC obstruction?**

A: As follows:

1. Chest X-ray (which shows mass lesion, bilateral hilar lymphadenopathy, mediastinal widening).
2. CT or MRI of chest.
3. Others (according to suspicion of causes)—
 - In bronchial carcinoma—sputum for malignant cells, CT or USG guided FNAC from lung lesion, bronchoscopy. Sometimes, mediastinoscopy, thoracotomy may be necessary.
 - In Lymphoma—FNAC or biopsy of LN.

Q: How will you **treat the case?**

A: Treatment should be given according to the cause:

- In bronchial carcinoma—Radiotherapy in non small cell carcinoma and chemotherapy for small cell carcinoma.
- If lymphoma—treat accordingly (usually chemotherapy).
- To relieve oedema—intravenous frusemide, head should be raised. Dexamethasone may be used.
- To relieve severe obstruction—balloon angioplasty and expandable metallic stent may be used (placed in SVC) as palliative measure.

INFERIOR VENA CAVAL OBSTRUCTION

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the patient. What are your findings? What else do you want to examine?

Presentation of a Case (Leg or Abdomen):

- Veins in the legs are engorged, flow is upwards.
- There are also engorged veins in abdomen, flanks and back, flow is upwards.
- Pitting oedema of the legs.

My diagnosis is **Inferior Vena Caval obstruction.**

Q: What is your **differential diagnoses**?

A: Varicose vein.

Q: What are the **causes** of IVC obstruction?

A: As follows:

- Thrombosis of IVC due to any cause (e.g., hypercoagulable state, myeloproliferative disease, oral pills).
- Compression of IVC (e.g., enlarged para-aortic lymph nodes, intra abdominal tumours, ascites, pregnancy).

Q: What **investigations** are done?

A: As follows:

- CBC, ESR.
- Doppler USG of leg veins.
- USG of whole abdomen.
- CT scan of abdomen.
- Venography.
- Laparoscopy and biopsy if needed.
- Other investigations according to suspicion of cause.



Engorged vein
in abdomen



Engorged vein
in chest



Engorged vein
in back



Engorged vein
in thigh

Q: How will you **treat** the case?

A: Treatment should be given according to cause.

1. Medical (see in DVT).
2. Treatment of primary cause.
3. Surgical—
 - IVC filter may be given to prevent pulmonary embolism.
 - Thrombectomy may be done.

HIRSUTISM

Instruction by the examiner:

- Look at the patient. What is your diagnosis? What else do you want to see?

Presentation of a Case (a Female Patient):

- There is hirsutism.
- Patient is obese with cushingoid face (if any).

Q: What are the **causes** in this case?

A: Mention the causes considering the age and physical appearance:

1. If cushingoid face—likely cause is Cushing's syndrome.
2. If patient is obese and young—likely cause is polycystic ovarian syndrome (PCOS).
3. Other causes:
 - Familial, racial and postmenopausal (In old age).
 - Drugs (see below).
 - Late-onset congenital adrenal hyperplasia.
 - Adrenal causes (carcinoma or androgen secreting adrenal tumour).
 - Ovarian cause (androgen-secreting ovarian tumour).
 - Idiopathic.

Q: What **else** do you want to see in this case?

A: As follows:

1. Hair in other parts of the body, chest and back (increased), hair in midline below the umbilicus to groin (increased), excess hair in the upper and lower limbs.
2. Evidence of **virilization**:
 - Male baldness (frontal baldness).
 - Male body habitus.
 - Deepening of voice.
 - Others (clitoromegaly, atrophy of breast, male pattern of pubic hair, acne, greasy skin).
3. Abdominal mass (PCOS, ovarian tumour, adrenal carcinoma).



Hirsutism



Hirsutism (in senility)



Hirsutism

Q: What **history** would you like to take?

A: As follows:

- Age of onset of hirsutism—In younger and early age, common cause is PCOS. So history of amenorrhoea, weight gain, infertility etc. should be taken. In elderly or middle age—hirsutism is most likely postmenopausal.
- Family history.
- If Cushing's syndrome is suspected—prolonged intake of steroid, weight gain.
- Drug history—Steroid, androgen, phenytoin, Cyclosporine, minoxidil.
- Menstrual history (amenorrhoea in PCOS).
- Rate of progression of hirsutism.
- Thinning of scalp hair.

N.B.: A good history regarding hirsutism is essential:

- *If the onset is shortly after menarche, tumour is unlikely.*
- *If it occurs in childhood, more chance of underlying disease.*
- *If menstruation is regular, more likely to be constitutional rather than tumour or other pathology.*
- *Greater the menstrual abnormality (irregular or cessation), more likely there is a serious disease (ovarian or adrenal).*
- *Rapid onset, prepubertal or late onset is suggestive of underlying disease (ovarian or adrenal).*
- *Increased libido and signs of virilization indicates increased androgen.*

READ THE FOLLOWING TOPICS IN RELATION TO HIRSUTISM

Q: What is **hirsutism**? What are the **causes**?

A: It is the excess growth of hair in women as male pattern due to excessive secretion of androgen. Hair growth occurs in beard or chin or moustache. Also in breast, chest, axilla, abdominal midline, pubic and thigh area. Increase hair growth indicates excessive androgen, either adrenal or ovarian in origin. **Causes** of hirsutism—

- Hirsutism without virilization.
- Hirsutism with virilization.

Hirsutism without virilization:

- Idiopathic (in most cases).
- Familial.
- Drugs (steroid, phenytoin, Cyclosporine, androgen, minoxidil, progesterone).
- Others—PCOS (mild), acromegaly, porphyria cutanea tarda.

Hirsutism with virilization:

- Ovarian causes—PCOS (severe case), androgen-secreting ovarian tumour, arrhenoblastoma.
- Adrenal causes—Late onset congenital adrenal hyperplasia, Cushing's syndrome, adrenal carcinoma or androgen-secreting adrenal tumour.

Q: How will you investigate a case of hirsutism?**A:** As follows:

- Good history (see above).
- History of drugs (see above).
- Family history.

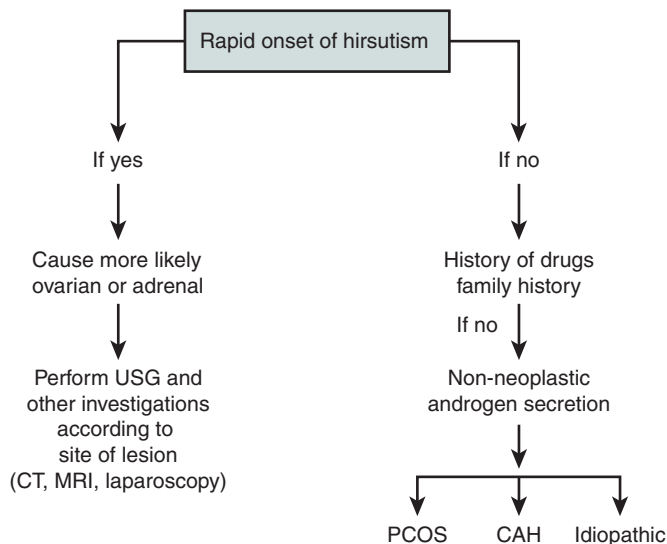
After exclusion of these, causes may be ovarian or adrenal. Next, USG of abdomen to see ovarian or adrenal mass.

A. If ovarian origin, following tests should be done—

- Blood for testosterone, LH, FSH and prolactin. If LH is high and FSH is normal or high (ratio of LH:FSH is 2 or 3), suggestive of PCOS. If testosterone is high (twice the normal) with low LH and FSH, it is unlikely to be PCOS and likely to be idiopathic hirsutism.
- Sex hormone binding globulin (SHBG)—high.
- Androgen—high, but testosterone is normal or low.
- Other tests—CT scan, MRI. Sometimes FNAC, even laparoscopy may be done.

B. If adrenal origin, following tests should be done—

- If adrenal carcinoma or adenoma—urinary 17-ketosteroid is high.
- Dexamethasone suppression test may be done (to see for failure of suppression).
- In congenital adrenal hyperplasia—serum 17-hydroxyprogesterone is high, and also high pregnanetriol and ACTH.
- Other tests—CT scan, MRI. Sometimes, FNAC, even laparoscopy may be done.

Another method of investigation:

Q: How to treat hirsutism?**A:** As follows:**1. Treatment of primary cause.** If due to drug, it should be stopped.**Local therapy:**

- Plucking, bleaching, depilatory cream, shaving, electrolysis, epilation.
- Topical eflornithine cream applied locally for 6 months is also effective.

2. Systemic therapy (given in severe cases):

- Cyproterone acetate (antiandrogen) 50–100 mg daily for 1–14 days of each cycle. In women of childbearing age, contraception is essential.
- Oestrogen (in oral contraceptive) is helpful in idiopathic or PCOS. It reduces free androgens by increasing SHBG.
- Metformin reduces the androgen level and may be given in treatment of hirsutism associated with insulin resistance (e.g., PCOS).
- Other antiandrogens: Spironolactone, flutamide or finasteride are also helpful.



Hypertrichosis in back



Hypertrichosis



Hypertrichosis in thigh and leg

Q: What is hypertrichosis? What are the causes?**A:** It is the generalized excess hair growth in any sex which is nonandrogenic in origin. Causes are:

- Familial.
- Sexual precocity.
- Hypothyroidism.
- Adrenal hyperplasia or neoplasm.
- Virilizing ovarian tumour.
- Drugs—minoxidil, Cyclosporine, androgen.

Q: What is the difference between hirsutism and hypertrichosis?**A:** As follows:

- Hirsutism is male pattern of hair growth in women due to excess of androgen.
- Hypertrichosis is generalized excess hair growth in any sex, which is nonandrogenic in origin.

Q: What are the causes of **decreased body hair**?

A: As follows:

- Cirrhosis of liver.
- Klinefelter's syndrome.
- Hypopituitarism.
- Bilateral testicular atrophy due to any cause (e.g., leprosy).

POLYCYSTIC OVARIAN SYNDROME

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the patient. What are your findings? (Usually hirsutism, obesity in a young girl)

Presentation of a Case (a Young, Obese Female Patient):

- There is hirsutism and patient is also obese.

My diagnosis is **Polycystic Ovarian Syndrome (PCOS)**.

Q: What are the **differential diagnoses**?

A: As follows:

1. Simple obesity.
2. PCOS.
3. Hypothyroidism.
4. Cushing's syndrome (other features are present).
5. Congenital adrenal hyperplasia (late onset. In such case, there is raised serum 17α hydroxyprogesterone).
6. Virilizing tumour of the adrenal or ovary (rapid onset of signs of virilization, very high serum testosterone).
7. Drugs (e.g., steroid, danazol, androgenic progestins).

READ THE FOLLOWING TOPICS IN RELATION TO PCOS

Q: What is **polycystic ovarian syndrome (PCOS)**?

A: It is syndrome in which there are multiple cysts in the ovary and hyperandrogenemia, characterized by amenorrhoea or oligomenorrhoea, obesity and hirsutism (triad). Other features are infertility (due to anovulation) and virilization (in severe cases).

PCOS is associated with increased LH due to abnormality of pulsatile **GnRH** secretion (there is chronic anovulation without specific underlying disease of adrenal, pituitary or ovary). It was originally called severe form of Stein–Leventhal syndrome.

Q: What are the **diagnostic criteria** of PCOS?

A: 2 of the following 3 features are required for PCOS to be diagnosed:

- Menstrual irregularities (oligomenorrhoea or amenorrhoea).
- Clinical or biochemical evidence of androgen excess.
- Multiple cysts in the ovaries (most readily detected by transvaginal ultrasonography).



PCOS (Hirsutism)



PCOS (Hirsutism)



Obesity in PCOS

Q: What **investigations** should be done to diagnose PCOS?

A: As follows:

1. USG of abdomen (it shows thickened capsule, multiple 3–5 mm cyst and hyperechogenic stroma).
2. Biochemical tests:
 - Serum testosterone—usually high (if markedly high, cause may be other than PCOS).
 - LH—high.
 - FSH—normal or low. Ratio of LH:FSH > 2 or 3.
 - Androgens—androstenedione and dehydroepiandrosterone are high.
 - SHBG—Low.
 - Prolactin—slightly increased, rarely greater than 1500 mU/L.
 - Oestrogen—oestradiol is usually normal.
3. To exclude other cause, investigations should be done according to suspicion:
 - Serum 17 α hydroxyprogesterone—high in late-onset congenital adrenal hyperplasia (CAH).
 - CT or MRI of adrenal—in suspected tumour.
 - Dexamethasone suppression test.
 - A short ACTH stimulation test with measurement of 17 α hydroxyprogesterone is done to diagnose CAH.

N.B. Raised ratio of LH:FSH is classical feature of PCOS, but no longer thought to be useful in diagnosis.

Q: How to treat PCOS?

A: As follows:

1. General measures:
 - Reduction of weight.
 - Regular exercise and diet control.
2. For hirsutism, as described in the topic 'hirsutism'.
3. For fertility:
 - Metformin—May improve ovulation and achieve conception.
 - Clomiphene 50 to 100 mg/day, from days 2 to 6 of cycle. Dexamethasone 0.5 mg at bedtime with clomiphene may increase the likelihood of ovulation by suppressing ACTH. Clomiphene is superior to metformin.
 - If no response to clomiphene, metformin may be added, 500 mg three times daily. It may enhance ovulation.
 - Prednisolone in reverse circadian rhythm (2.5 mg in the morning and 5 mg at bedtime) may suppress pituitary ACTH, upon which adrenal androgen partly depend. With this therapy, regular ovulatory cycle often ensue.
4. For menstrual disturbance:
 - Metformin 500 mg three times daily. Also may improve hirsutism and obesity.
 - Cyclical low dose oestrogen or progesterone.
 - Patient who does not desire pregnancy should get medroxyprogesterone 10 mg daily orally for first 10 days of each month. It ensures regular shedding of endometrium.
 - Wedge resection or laser surgery of ovary or laparoscopic ovarian drilling may be done in some cases.
 - Oral contraceptive pill may be helpful.
5. For obesity—Metformin may be used.

N.B. Adrenal androgen is under control of ACTH and ovarian androgen is under control of LH.

Q: What are the complications in PCOS?

A: As follows:

- Hyperinsulinaemia and insulin resistance.
- Glucose intolerance.
- Type 2 DM.
- Hypertension, dyslipidaemia and cardiovascular risk.

LEG ULCER

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the leg or, examine the leg.

Look at the following points carefully:

- Site of ulcer (one or both legs or feet or tip of toes).
- Single or multiple.
- Margin (irregular, raised, undermined, everted, punched out).
- Floor (granulation or necrotic tissue, black).
- Any slough or gangrene.
- Dry or oozing (pus or serous fluid).
- Any blister (intact or rupture).
- Surrounding area (healthy or pigmented).
- Temperature (cold or warm).
- Pulse (absent, sluggish or bounding).
- Sensation (light touch, pain, vibration and position sense).



Leg ulcer in SLE



Varicose ulcer



Leg ulcer



Ulcer in heel

Presentation of a Case:

- There is one ulcer (or multiple ulcers), involving one or both shin of legs or feet, with a clear margin. Some parts are necrosed or gangrenous, with oozing.
- Leg is cold, pulse is absent, sensation is normal.
- Joint abnormality (mention, if any).

Q: What do you think are the **causes** of leg ulcer?

A: Mention the causes according to the age of the patient:

If the patient is middle-aged or elderly, the causes are:

- Trauma.
- Peripheral vascular disease (due to atherosclerosis).
- Diabetes Mellitus.
- Peripheral neuropathy.
- Infection (TB, pyogenic infection, leprosy, leishmaniasis).
- Pyoderma gangrenosum.
- Rheumatoid arthritis, SLE.

If the patient is young, the causes are:

- Trauma.
- Diabetes Mellitus.
- Haematological diseases (e.g., sickle cell anaemia, thalassaemia, hereditary spherocytosis).
- Collagen disease (SLE, RA, Felty's syndrome).
- Infection (As above)
- Buerger's disease, Raynaud's disease.

Q: What history do you like to take in leg ulcer?

A: History of trauma, smoking, DM, hypertension, evidence of infection, collagen diseases.

Q: What investigations should be done in leg ulcer?

A: As follows:

- CBC, ESR.
- Urine RME.
- Blood sugar.
- Lipid profile.
- X-ray of chest (to exclude tuberculosis).
- Pus (if any) for C/S, AFB, LD bodies.
- Doppler USG of lower limb vessels.
- X-ray of leg (exclude osteomyelitis, also calcification in artery may be seen).
- Arteriography.
- Others: According to suspicion of causes, e.g., ANA, cold agglutinin and RA test.
- Biopsy.

Q: How to treat leg ulcer?

A: As follows:

- Smoking should be stopped.
- Control of DM, hypertension, obesity (if any).
- Treatment of primary cause.
- Local care (cleaning, removal of necrotic tissue and dressings).
- Antibiotic, if any infection.
- Consult with chiropodist.
- Low-dose aspirin.
- In some cases, surgery (balloon dilatation) and if necessary, amputation.
- Education to—Avoid walking bare foot, avoid tight shoes, use appropriate footwear, crutch may be used to avoid weight bearing, cutting toe nails carefully, blisters should be cleared.

READ THE FOLLOWING TOPICS IN RELATION TO LEG ULCER

Causes of leg ulcer:

- Traumatic (injury, burn, radiation).
- Infection (pyogenic, TB, leprosy, leishmaniasis).
- Arterial—Atherosclerosis or other peripheral vascular disease (Buerger's disease, Raynaud's disease).
- Venous ulcer occurs usually due to varicose vein.
- Neuropathic ulcer (due to DM, tabes dorsalis, syringomyelia, leprosy, polyneuropathy due to any cause).
- Collagen disease (SLE, RA, Felty's syndrome, cryoglobulinaemia, polyarteritis nodosa).
- Haematological (sickle cell anaemia, thalassaemia, hereditary spherocytosis, paroxysmal nocturnal haemoglobinuria, thrombotic thrombocytopenic purpura and macroglobulinaemia).
- Neoplastic (squamous cell carcinoma, basal cell carcinoma, malignant melanoma, lymphoma and Kaposi's sarcoma).
- Pyoderma gangrenosum.

N.B.: Following are the characters of different types of ulcers:

- *Arterial ulcer occurs more on tip of toes, dorsum of foot, usually tender, cold skin, loss of hair and absent or reduced pulse.*
- *Venous ulcer is usually around malleoli, in the medial lower third of leg, oedematous. There may be wet gangrene, pigmentation and eczema, usually painless unless infected.*
- *Neuropathic ulcer is usually painless, sites are usually pressure points such as beneath heel, beneath 1st and 4th metatarsal head.*

PYODERMA GANGRENOSUM

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the foot or leg. What are your findings? What is the likely diagnosis?

Presentation of a Case (Supposing Right Foot):

- In the lateral aspect and dorsum of foot, there is a large necrotic ulcer with ragged bluish-red, gangrenous overhanging margin, purulent surface with pustules and plaque.
- Surrounding skin is indurated and erythematous.



Pyoderma gangrenosum
on foot



Pyoderma gangrenosum
on foot and leg



Pyoderma
gangrenosum on leg



Pyoderma gangrenosum
on finger

My diagnosis is **pyoderma gangrenosum**.

Q: What are the **differential diagnoses**?

A: As follows:

- Traumatic ulcer.
- Venous ulcer.
- Infection (TB, pyogenic infection, leprosy, leishmaniasis).
- Vasculitis (polyarteritis nodosa, Behcet's syndrome, Wegener's granulomatosis).
- Haematological (sickle cell anaemia).
- Neoplastic (squamous cell carcinoma, basal cell carcinoma, cutaneous lymphoma).

Q: Ask one **question** or what **history** do you like to take?

A: History of diarrhoea or bloody diarrhoea (suggestive of inflammatory bowel disease).

READ THE FOLLOWING TOPICS IN RELATION TO PYODERMA GANGRENOSUM:

Q: What is **pyoderma gangrenosum**?

A: It is a disease of unknown aetiology characterized by non-infective, necrotizing ulceration, starts as a nodule or pustule, that frequently ulcerates. Ulcer may be single or multiple with clear bluish-black (gangrenosum) undermined edge and purulent surface (pyoderma). Common in legs, in the shin but may occur anywhere in the body. It is common in adults (25 to 54 years). Diagnosis is clinical, biopsy shows inflammatory neutrophilic infiltrate, occasionally vasculitis.

Q: What is the **pathogenesis** of pyoderma gangrenosum?

A: Actual pathogenesis is unclear, there is depression of immune system. Failure of macrophage to respond to tissue injury or to clear the obnoxious agent is another factor.

Q: What are the **causes**?

A: As follows:

Causes of pyoderma gangrenosum:

- Inflammatory bowel disease: Ulcerative colitis (common), less in Crohn's disease.
- Rheumatoid arthritis.
- Polycythaemia rubra vera.
- Chronic granulocytic leukaemia (also in acute granulocytic leukaemia, Hairy cell leukaemia).
- Multiple myeloma.
- Monoclonal gammopathy, IgA type.
- Wegener's granulomatosis.
- Chronic active hepatitis.
- Idiopathic in >20% cases.

Q: What **investigations** will you do?

A: As follows:

1. CBC, ESR.
2. Blood sugar.
3. Biopsy from the lesion.
4. Other investigations according to suspicion of cause:
 - For IBD—Barium enema, colonoscopy.
 - For collagen disease—ANA, anti-dsDNA, anti-phospholipid antibody.
 - For vasculitis—pANCA, cANCA.
 - For myeloma—Protein electrophoresis, bone marrow.

Q: How to treat pyoderma gangrenosum?

A: As follows:

1. Treatment of underlying diseases.
2. General measures:
 - Control of infection.
 - Local dressing
 - Analgesic for pain.
3. Topical:
 - Corticosteroid. Triamcinolone may be injected into the ulcer edge (alone or with systemic treatment).
 - Tacrolimus may be given.
4. Systemic:
 - Oral prednisolone. In some patients, methylprednisolone 1 gm I.V. for 3 days, followed by oral prednisolone.
 - Minocycline 100 mg/day may help to reduce the dose of steroid.
 - Immunosuppressive drug—Cyclosporine, tacrolimus or azathioprine may be used.
 - Anti-TNF α (infliximab, etanercept) may be used, if others fail.
 - Dapsone may be used in milder cases.
 - Other drugs: Colchicine, clofazimine, cyclophosphamide, mycophenolate mofetil may be used.

N.B.: 50% patient of pyoderma gangrenosum have ulcerative colitis, indicates severe disease. It may precede the onset of inflammatory bowel disease. Healing parallels with cure of ulcerative colitis and colectomy causes rapid healing.

DIABETIC FOOT

Instruction by the examiner:

- Look at the foot of this diabetic patient.
- Perform the general examination of this diabetic patient.

Look carefully the following points:

Inspection:

- Ulcer (site, single, multiple, oozing, gangrene, surrounding skin).
- Look at the tip of all toes, sole and spaces between the toes.
- If gangrene is present, see whether it is dry or wet, demarcation between healthy and unhealthy skin.
- Colour change of skin and hair loss.
- Amputation of toe (may be).
- Pigmented scar, small round plaques with raised border in a linear fashion over shin (diabetic dermopathy).
- Necrobiosis lipoidica diabetorum (central yellow with raised margin, telangiectasia at the margin).
- Joints (Charcot joint or joint swelling).
- Thigh wasting, atrophy or hypertrophy (insulin therapy).

Palpation: Ask the patient whether the foot is sore.

- Temperature (warm or cold, compare with other foot).
- Pulse (arteria dorsalis pedis, posterior tibial), if reduced, absent or bounding.
- Sensation, reduced or absent (see light, touch, pain, joint sense).
- Vibration and position sense (may be lost due to the posterior column lesion called diabetic pseudotabes).
- Reflex, reduced or absent, see also plantar response.
- In some cases, test for proximal myopathy (diabetic amyotrophy, which shows asymmetrical wasting of thigh).

Q: What is diabetic foot?

A: Diabetic foot is a group of disorders that occurs as complication of diabetes mellitus. Presence of multiple pathology such as infection, diabetic foot ulcer and neuropathic osteoarthropathy is called **diabetic foot syndrome**.

Q: What are the features of diabetic foot? How to manage diabetic foot?

A: As follows:

1. Neuropathic: Ulcer (plantar), sepsis, abscess, osteomyelitis, digital gangrene, Charcot joint, high arched and clawing of toes.
2. Ischaemic: Ulcer, sepsis, gangrene.

Management: Prevention is the main step. Along with good control of diabetes, following measures should be taken:

1. Advice to all diabetic patients:
 - Inspect and wash feet every day.
 - Moisturization of skin, if dry.
 - Cut toe nails regularly, very carefully.
 - Wear suitable good-fitting shoes.
 - Check footwear for foreign bodies.
 - Change socks or stockings every day.
 - Avoid walking barefoot.
 - Cover minor cuts with sterile dressings.
 - Do not burst blisters.
 - Avoid over-the-counter corn or callus remedies.
 - Keep feet away from heat (e.g., hot water, hot sand, fire, radiation).
2. Additional advice to high-risk patients:
 - Do not attempt corn removal.
 - Avoid high and low temperature.
3. Involve a podiatrist in the care of the patient.
4. Special footwear should be used in Charcot neuroarthropathy.

DIABETIC ULCER

Presentation of a Case (Supposing Right Foot):

- There is an ulcer involving the dorsum of right foot, some part is gangrenous, with red irregular margin and also some oozing.
- There is also pigmented area surrounding the ulcer with loss of hair and shininess.
- Foot is cold, pulse is absent and loss of sensation in foot and leg, also loss of vibration and position sense.

This patient has evidence of peripheral neuropathy and ulcer, the **more likely diagnosis** is diabetic ulcer.

Q: What are the differential diagnoses?

A: As follows:

- Diabetic foot ulcer.
- Pyoderma gangrenosum.
- Infective (pyogenic, TB, leprosy and leishmaniasis).
- Buerger's disease.
- Vasculitis—SLE, polyarteritis nodosa and RA.



Diabetic ulcer in dorsum
(with gangrene and
oozing)



Diabetic ulcer in dorsum
(with infarction and
cellulitis)



Diabetic ulcer in sole
(with gangrene)



Diabetic ulcer in sole
(without gangrene)

Q: What are the causes of ulcer in DM?

A: As follows:

- Ischaemia.
- Neuropathy.
- Combined ischaemia and neuropathy.
- Secondary infection.
- Trauma.

N.B.: If the ulcer is painful, the cause is vasculitis and if it is painless, the cause is neuropathic.

Q: What is the pathology of ischaemic ulcer?

A: Usually macrovascular, associated with atherosclerosis.

Q: What are the **findings**, if the ulcer is due to **combined** neuropathy and ischaemia?

A: In such case, the findings are:

- Ulcer is on foot, callosities and pressure points.
- Loss of arch of foot.
- Sensory loss of all modalities in stocking pattern.
- Loss of pulsation.
- Foot is cold, shiny with loss of hair.

Q: What are the **differences** between ischaemic and neuropathic ulcer or what are the features of neuropathic and ischaemic ulcer?

A: As follows:

Features	Neuropathic Ulcer	Ischaemic Ulcer (Arterial)
Symptoms	No pain. Paraesthesia or tingling may be present.	Pain, history of claudication.
Foot	High arched, clawing of toes, no trophic change	Rubor, trophic changes (atrophy and loss of hair)
Area	Warm, dry and pink	Cold, shiny
Pulse	Bounding	Absent or reduced
Sensation	Reduced or absent	Normal
Ulcer	Painless and mostly plantar	Painful, over heels and toes
Reflex	Reduced or absent, equivocal plantar response	Normal

Q: How to **investigate** diabetic ulcer?

A: As follows:

- CBC.
- Blood sugar.
- Urine RME.
- X ray of the affected part.
- Doppler USG of the lower limb vessels.
- C/S from pus, if any.

Q: How to **treat** a case of diabetic ulcer?

A: As follows:

- Good control of DM.
- Smoking should be stopped.
- Local dressing and removal of dead tissue.
- Antibiotic to control secondary infection.
- Consult with chiropodist.
- Surgery may be required (removal of callus, amputation or angioplasty).
- Patient's education: Avoid barefoot, tight shoes, careful cutting of nails, avoid weight bearing.
- Other measures: As in diabetic foot.
- Liaison should be maintained among physician, chiropodist and surgeon.
- If localized area of occlusion—either bypass surgery or angioplasty may be needed.

Causes of neuropathic ulcer:

- Diabetes mellitus.
- Leprosy.
- Polyneuropathy (due to any cause).
- Tabes dorsalis.
- Syringomyelia.
- Amyloidosis.
- Porphyria.
- Progressive sensory neuropathy.

DIABETIC AMYOTROPHY

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the thigh. What are your findings?

Presentation of a Case:

- There is wasting in right or left thigh, with tenderness of the thigh muscles, muscle power and tone are diminished.
- Loss of knee jerk, but no loss of sensation.
- Patient is cachexic or emaciated.

My diagnosis is **Diabetic amyotrophy**.

Q:What is **diabetic amyotrophy**?

A: It is a type of motor neuropathy in diabetic patient, characterized by asymmetrical wasting of muscles, usually involving the quadriceps (also in the shoulder). It may be the first presentation of DM.

Q:What are the **features** of diabetic amyotrophy?

A: The patient usually presents with severe pain with wasting of quadriceps, also in the shoulder. Hyperaesthesia or paraesthesia is common, affected area may be very tender, the patient is occasionally cachexic (neuropathic cachexia) and extremely ill, unable to get out of bed. There is reduction of muscle power, tone, loss of knee jerk with occasional extensor plantar response on the affected side. CSF protein is increased.

Q:Where is the **site of lesion** or **cause** of diabetic amyotrophy?

A: It is thought to involve acute infarction of lower motor neuron of lumbosacral plexus.

Q:In which **type** of diabetes it is common?

A: It is more common in type 2 DM, also common in elderly.

Q:How to **treat** diabetic amyotrophy?

A: As follows:

- Good control of DM.
- Intensive insulin therapy.
- For pain—amitriptyline, imipramine or carbamazepine. Aldose reductase inhibitor may help.

Q:What is the **prognosis**?

A: Prognosis is good, usually recovers, but may take a long time (over months to 2 years).



Diabetic amyotrophy (Left thigh)



Diabetic amyotrophy (Right thigh)

Q: What are the causes of **unilateral** wasting of leg?

A: As follows:

- Diabetic amyotrophy.
- Old poliomyelitis.
- Arthritis or trauma.
- Cerebral palsy.
- Disc prolapsed (PLID).

LIPODYSTROPHY OF THIGH

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the thigh. What are your findings?

There may be two types of findings in the thigh, together called lipodystrophy:

- Lipoatrophy.
- Lipohypertrophy.

Presentation of a Case (Lipoatrophy or Lipohypertrophy of Thigh):

- There is atrophy or wasting of muscle of thigh with multiple needle puncture marks.
- Or, there is hypertrophy of thigh muscles with multiple needle puncture marks.

Diagnosis is **lipoatrophy** or **lipohypertrophy**.

Q: What is the underlying **diagnosis**?

A: The patient is diabetic, receiving insulin injection.

Q: What is **lipoatrophy**? What are the **causes**?

A: It is the localized atrophy of subcutaneous fat due to repeated injection of unpurified animal insulin caused by immunogenic component of insulin. Treated by injection of pure human insulin at the margin and centre of the affected area, which results in restoration of normal contour. It is rare now due to less use of animal insulin.

Causes of lipoatrophy of skin:

- DM (receiving insulin injection).
- Localized scleroderma or morphoea.
- Chronic relapsing panniculitis.
- Mesangiocapillary glomerulonephritis.
- HIV.



Diabetic lipoatrophy



Diabetic lipohypertrophy



Diabetic dermopathy



Diabetic bullae

Q: What is **lipohypertrophy**?

A: It is the localized hypertrophy of subcutaneous fat due to repeated injection of purified insulin at the same site. It is caused by continued lipid synthesis at the affected site, and is treated by changing the site of injection.

NECROBIOSIS LIPOIDICA DIABETICORUM

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the leg. What are your findings?

Presentation of a Case:

- There is sharply demarcated, atrophied skin or plaque in the skin of shin with shiny surface and waxy yellow centre, brownish-red margin with surrounding telangiectasia.

Diagnosis is **necrobiosis lipoidica diabeticorum**.

Q: What are the **differential** diagnoses?

A: As follows:

- Necrobiosis xanthogranuloma.
- Cutaneous sarcoidosis.
- Localized scleroderma.
- Polyarteritis nodosa.

Q: What is **necrobiosis lipoidica diabeticorum**?

A: It is characterized by plaque-like lesion with central yellowish area surrounded by brownish border on the anterior surface of leg. May be shiny, atrophic skin with telangiectasia. Fibrosis with scarring from previous ulceration may be seen. This is a rare finding in DM (<1%), may be in prediabetic and in 50%, without diabetes. But 85% cases with necrobiosis lipoidica diabeticorum develop DM. It is 2 to 3 times common in females, usually in young or early middle life. Cause is unknown, may be due to small vessel damage.

Histology shows necrosis of collagen, infiltration with epithelioid cells, giant cells with glycogen and lipid deposition.



Necrobiosis lipoidica diabeticorum



Necrobiosis lipoidica diabeticorum



Necrobiosis lipoidica diabeticorum (Early stage)

Treatment:

- Good control of DM.
- Protection of skin, avoid trauma.
- Dressing, local application or injection of steroid may be helpful.
- Psoralen + UVA (PUVA) may be helpful.
- Surgery with skin grafting.
- Low-dose aspirin, occasionally pentoxifylline may be helpful.
- Laser therapy.

Q: What is diabetic dermopathy?

A: It is characterized by atrophic, round or oval shaped, reddish brown or pigmented patch in skin, commonly in the pretibial area, precipitated by trauma associated with neuropathy. Initially it may be scaly but then flattens out and becomes indented. No specific treatment is necessary, improves with good control of blood sugar.

Q: What are the skin changes in DM?

A: As follows:

- Necrobiosis lipoidica diabetorum.
- Diabetic dermopathy.
- Ulcer or gangrene.
- Secondary infections (boil, carbuncle and candidiasis).
- Acanthosis nigricans.
- Xanthelasma and eruptive xanthomata.
- Granuloma annulare.
- Lipoatrophy and lipohypertrophy.
- Diabetic bullae.
- Others: Vitiligo, xanthoma and peripheral anhidrosis.
- Diabetic rubeosis (redness of face, hands and feet, due to diabetic microangiopathy).

N.B. Necrobiosis lipoidica may be found in non diabetic case also (e.g., Rheumatoid arthritis). So, the term 'necrobiosis lipoidica' is used rather than necrobiosis lipoidica diabetorum.

UNILATERAL OR BILATERAL LEG SWELLING

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the lower limbs. Or, examine the lower limbs.

Look carefully at the following points:

Inspection:

- Swelling, extent of swelling (right or left or both).
- Veins (engorged or varicose veins).
- Skin colour, scratch mark, pigmentation, purpura, hair change, trophic ulcer.
- Joint swelling, clubbing and cyanosis, also back of the leg.

Palpation:

- Temperature (warm or cold).
- Pulse (arteria dorsalis pedis, posterior tibial and popliteal artery).
- Oedema (pitting or nonpitting).
- Calf tenderness and localized swelling (may be present in DVT, ruptured Baker's cyst).
- Homans sign (may be dangerous, there is risk of pulmonary embolism).
- Associated lymph nodes (popliteal, inguinal).

Presentation of a Case 1 (Supposing Right):

- Right leg is swollen. Skin is rough, scaly and thick with loss of lustre and hair. There is excoriation or scratch mark.
- Local temperature is normal (or cold or warm)
- Oedema is present which is non-pitting.
- Arterial pulse is normal and there is no lymphadenopathy.

Diagnosis is **lymphoedema**, which may be due to:

- Filariasis.
- Trauma.
- Surgery.
- Radiation.
- Recurrent lymphangitis or cellulitis.
- Neoplasm (usually pelvic site).
- Primary lymphoedema.



Lymphoedema of left lower limb



Unilateral lymphoedema (left)



Bilateral leg swelling



Bilateral lymphoedema

Q: What are the **differential diagnoses** of unilateral leg swelling?

A: As follows:

- Lymphoedema.
- DVT.
- Angioneurotic oedema.
- Ruptured Baker's cyst.
- Chronic venous insufficiency.
- Traumatic.
- Compartment syndrome following trauma or surgery (requires immediate fasciotomy).

N.B. Unilateral swelling in arm may occur following mastectomy or radiotherapy in chest.

Q: How will you **investigate** a patient with unilateral leg oedema?

A: As follows:

1. CBC (high eosinophil in filariasis).
2. Urine RME (urine may be whitish due to chyluria).
3. Other according to suspicion of cause:
 - Colour Doppler USG of the affected limb (to exclude DVT or venous insufficiency).
 - For lymphoedema (see below).

Q: What is the **mechanism of nonpitting oedema**?

A: Normally, small amount of albumin filtered through the capillaries is absorbed through lymphatics. In lymphatic obstruction, water and solutes are reabsorbed into the capillaries, but the protein remains, which causes fibrosis and the area becomes hard or thick.

Presentation of a Case 2 (Bilateral Leg Swelling):

- Both the legs are swollen, with pitting oedema.
- Local temperature is normal (or warm).
- Arterial pulse is normal.

Bilateral pitting oedema, which may be due to:

- CCF.
- Nephrotic syndrome.
- Hypoproteinaemia.
- Drugs (calcium channel blockers, such as nifedipine or amlodipine).
- Inferior vena caval obstruction.

READ THE FOLLOWING TOPICS IN RELATION TO LEG OEDEMA

Q: What are the **causes** of non-pitting oedema?

A: As follows:

- Lymphoedema due to any cause.
- Myxoedema.

Q: What are the **causes** of pitting oedema?

A: As follows:

- CCF.
- Nephrotic syndrome.
- Cirrhosis of liver (in advanced stage).
- Hypoproteinaemia.
- Inferior vena caval obstruction.
- Iliac vein thrombosis.
- Pregnancy.
- Drugs (calcium channel blockers, such as nifedipine or amlodipine).

Q: How will you **investigate** a patient with bilateral leg oedema?

A: As follows:

1. CBC.
2. Urine RME.
3. Serum creatinine.
4. Other according to suspicion of cause:
 - If CCF—ECG, chest X-ray, echocardiogram.
 - If nephrotic syndrome—Serum total protein, A:G ratio, 24-h urinary protein, renal biopsy if needed.
 - If myxoedema—TSH, FT₃, FT₄.
 - Ultrasonogram of whole abdomen.
 - Duplex study of both lower limbs.

Q: What are the causes of **acute unilateral** leg swelling?

A: As follows:

- Deep venous thrombosis.
- Ruptured Baker's cyst.
- Cellulitis.
- Trauma.
- Angio-oedema.

Causes of Lymphoedema:

1. Primary:
 - Secondary to agenesis or hypoplasia.
 - Hereditary (Milroy's disease).
 - Associated with Turner's syndrome, Noonan's syndrome and yellow nail syndrome.
2. Secondary:
 - Recurrent lymphangitis or cellulitis.
 - Filariasis.
 - Trauma.
 - Tuberculosis.
 - Neoplasm.
 - Surgery (in the arm, it may be due to mastectomy).
 - Radiation.
 - Burn.

Q: What investigations do you suggest in lymphoedema (filariasis)?

A: As follows:

1. CBC, ESR (eosinophil may be high in filariasis).
2. Blood film to see filaria (usually at night, for *Wuchereria bancrofti* and *Brugia malayi*). Also, found in chylous and hydrocoele fluid.
3. Provocation test (by giving diethylcarbamazine, 50 mg orally, then blood film should be seen for filaria after 30 minutes).
4. CFT or ICT for filaria.
5. Filarial antigen detection.
6. Lymphoscintigraphy.
7. Lymphangiogram.
8. Other investigations to exclude other disease:
 - Chest X-ray.
 - MT.
 - USG of whole abdomen.
 - Doppler USG of lower limbs (to exclude DVT).
 - USG of scrotum ('filarial dance sign', pathognomonic for nest of filarial parasites).
 - CT scan or MRI of abdomen.

Q: How to treat lymphoedema?

A: No curative treatment. Mainly supportive to reduce the swelling and control discomfort.

1. Intermittent elevation of the extremity by placing pillows, mainly during sleeping.
2. Compression treatments:
 - Elastic sleeves or stockings.
 - Bandages—The extremity is wrapped tightly to remove lymph out of the limb.
 - Massaging the affected part either by hand or by pneumatic compression.
 - Exercise.
3. Surgical—May be used to remove excess fluid and tissue in severe cases.
4. Secondary infections should be treated with antibiotics.

Q: How will you treat filariasis?

A: In active lymphatic filariasis (defined by microfilaraemia, antigen positivity or adult worms on ultrasound) should be treated with—

- Diethylcarbamazine (DEC)—6 mg/kg daily for 12 days. Or,
- Albendazole (400 mg bid for 21 days) or albendazole and DEC both are given daily for 7 days, doxycycline (100 mg bid for 4 to 8 weeks). Addition of DEC to 3 weeks course of doxycycline is alternative regimens with macrofilaricidal efficacy.
- A single dose of albendazole (400 mg) combined with DEC (6 mg/kg) or ivermectin (200 µg/kg) for eradication campaign.
- Treatment of *Wolbachia* with doxycycline (200 mg/day) for 4 to 8 weeks provides additional benefit by eliminating the bacteria

N.B.: This treatment should be repeated every 6 months, if there is persistent symptoms with high eosinophil in blood.

ANGIOEDEMA

Instruction by the examiner:

- Look at the patient. What is the diagnosis?

Presentation of a Case:

- The face or lips or hand are swollen with non pitting oedema or periorbital swelling in left eye.
- Local temperature is raised.

My diagnosis is **angioedema**.



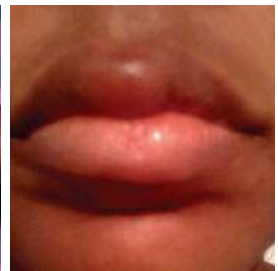
Angioedema (Face)



Angioedema (Left eyelid)



Angioedema (Hand)



Angioedema (Lips)

Q: What is **angioedema**?

A: Angioedema is the episodic, localized, non-pitting swelling of submucous or subcutaneous tissues. 2 types: hereditary and acquired.

1. Acquired angioedema is mostly due to allergy, type 1 hypersensitivity reaction. There may be localized swelling of face, eyelid, lip, tongue, hands. In severe case, there may be wheezing, shortness of breath, nausea, abdominal pain. Mouth and laryngeal involvement may cause severe suffocation, can be life-threatening.

Treatment—

- Mild to moderate case—Anti histamine (cetirizine, loratidine), offending agents should be avoided.
- Severe case (If mouth or laryngeal involvement)—I.M. Adrenaline, I.V. steroid should be given.

2. **Hereditary angioedema** is a disorder inherited as autosomal dominant due to C1-esterase inhibitor deficiency (C1-INH). There is involvement of the blood vessels. Family history is present. Attack is usually recurrent. Episodes of oedema in the skin of face, limbs and mucosa of the larynx can occur. Laryngeal oedema may be life threatening. Recurrent abdominal pain may occur. Non-hereditary form may occur in lymphoma or SLE.

Q: What **investigations** are done in **hereditary angioedema**?

A: Diagnosis is clinical. The followings should be done:

- Serum C2 and C4 (both low).
- Measurement of C1 esterase inhibitor (C1-INH, which is low).

Q: How to **treat** hereditary angioedema?

1. In acute attack:
 - C1-esterase inhibitor (C1-INH) concentrate and fresh frozen plasma should be given, if available.
 - 2 new drugs icatibant and ecallantide may be used for severe acute attack.
2. To prevent recurrent attack—danazol or stanozolol may be given. It synthesizes C1 esterase inhibitor by stimulating the liver (It may cause fluid retention, menstrual irregularity, obesity and androgenic effect. Should not be used in children.)

N.B. Remember the following points:

- *Antihistamines, adrenaline and steroid are often ineffective in hereditary angioedema.*
- *Helicobacter pylori can trigger abdominal attacks. Treatment of H. pylori will decrease abdominal attacks.*

DEEP VENOUS THROMBOSIS (DVT)

Instruction by the examiner:

- Perform the general examination of the patient.
- Examine the lower limbs. Or, look at the legs, what are your findings?

Presentation of a Case 1 (Supposing Left Lower Limb):

- Left leg is swollen up to the knee. It is red, warm with pitting oedema and tenderness in the calf muscles. Superficial veins are prominent and tender.
- Homans sign is positive.

My diagnosis is **deep venous thrombosis (DVT)**.



DVT (left lower limb)



DVT (right lower limb)



DVT (right upper limb)

Q: What are the other possibilities?

A: As follows:

- Cellulitis.
- Ruptured Baker cyst.
- Post-traumatic and calf haematoma.

Q: What single investigation would you suggest?

A: Doppler USG of lower limb vessels.

Q: What is Homans sign?

A: Dorsiflexion of foot causes pain in calf muscle (unreliable sign). This test is dangerous because of risk of pulmonary embolism. It is also positive in ruptured Baker cyst, trauma and inflammation in calf muscle.

Presentation of a Case 2 (Supposing Right Upper Limb):

- Right upper limb is swollen. It is red, warm with pitting oedema. Superficial veins are prominent and tender.

My diagnosis is **deep venous thrombosis (DVT)** involving the upper limb.

Q: What is the **likely** cause?

A: Axillary vein thrombosis.

Q: What **single investigation** would you suggest?

A: Doppler USG of upper limb vessels.

Q: What are the **common sites** of DVT?

A: Calf muscle veins, popliteal, femoral and iliac veins (swelling up to thigh, femoral or iliac vein thrombosis).

Q: What **history** should be taken in a patient with DVT?

A: As follows:

- Onset: Acute, chronic or recurrent.
- History of immobilization: Prolonged bed rest, trauma, surgery, CVD.
- History of air travel.
- Drug history (OCP).
- History of any primary disease like polycythaemia rubra vera, malignancy, SLE, nephrotic syndrome.
- Family history.

READ THE FOLLOWING TOPICS IN RELATION TO DVT

Q: What are the **causes** of DVT? What are the predisposing factors for DVT?

A: Causes are (**Virchow's law**):

1. **Stasis:** Causes are:
 - Prolonged bed rest or immobilization (after acute myocardial infarction, cerebrovascular accident, fracture).
 - Postoperative (prostatectomy, hip or pelvic surgery, lower limbs surgery).
 - Pregnancy and puerperium.
2. **Vascular endothelial damage:** Causes are:
 - Trauma, surgery (commonly after prostatectomy, abdominal or pelvic surgery).
 - Varicose vein.
 - Buerger's disease, Raynaud's disease.
3. **Hypercoagulability:** Causes are:
 - Oral contraceptive pill.
 - SLE (due to antiphospholipid syndrome).
 - Nephrotic syndrome.
 - Haematological disease (polycythaemia rubra vera, paroxysmal nocturnal haemoglobinuria, myelofibrosis, essential thrombocythaemia, DIC).
 - Internal malignancy (e.g., carcinoma of pancreas, lung, ovary and stomach).
 - Anticoagulant deficiency (antithrombin III, proteins C and S, factor II).
 - Others—Factor V Leiden, septicaemia.

Q: What are the causes of **recurrent DVT**?

A: As follows:

- Antiphospholipid antibody syndrome, SLE.
- Protein S, C, antithrombin III deficiency.
- Factor V Leiden.
- Polycythaemia rubra vera.
- Oral contraceptive pill.
- Malignancy.

Q: How to **diagnose DVT**?

A: As follows:

- Doppler USG of lower limb vessels (to note velocity of blood flow in the vein).
- D-dimer (high).
- Venography (confirmatory).

N.B.: High D-dimer may occur in pulmonary embolism, MI, pneumonia, sepsis. But low D-dimer (<500 ng/mL) excludes DVT in low-risk patients.

Q: What **other investigations** should be done to find out cause?

A: As follows:

- CBC, ESR (to see polycythaemia rubra vera).
- Antithrombin III, protein C or S.
- Factor V Leiden level.
- ANA, anti-ds-DNA, antiphospholipid antibody (for SLE).
- Serum homocysteine level.
- X-ray chest and USG of whole abdomen (to see malignancy).

Q: What are the **complications** of DVT?

A: As follows:

- Pulmonary embolism (commonly from thrombosis in ileo-femoral vein, less commonly from below-knee thrombosis).
- Venous gangrene.
- Post-phlebitic syndrome (chronic DVT results in permanently swollen limb with ulceration).

Q: How to treat DVT?**A:** As follows:

1. General treatment:
 - Bed rest and relief of pain by analgesic.
 - Use of elastic stockings from midfoot to below knee (in calf thrombosis).
 - Intermittent elevation of foot during day and night (above the heart level).
 - Mobilization slowly, when the patient is fully anticoagulated.
2. Anticoagulation: Above knee thrombosis must be anticoagulated (as more chance of pulmonary embolism). Below knee DVT should also be anticoagulated for 6 weeks.
3. If anticoagulation is contraindicated or in recurrent pulmonary embolism—IVC filter should be given.

Anticoagulant is used as follows:

1. Unfractionated heparin—initially I.V loading dose 5,000 I.U, then continuous infusion 1,000 to 2,000 IU/hour (20 IU/kg/hour) with infusion pump. APTT should be done (It should be 1.5 to 2.5 times of control), given for 5 days.
2. Low-molecular-weight heparin—enoxaparin, 1.5 mg/kg/day subcutaneously. Dose is reduced in renal failure.
3. Oral anticoagulant—
 - Warfarin should be started with heparin (It takes 48 h for its full effect), 10 mg daily for 2 days, then maintenance dose 3 to 9 mg, according to INR (target INR should be 2.5).
 - If single episode of thromboembolism, it should be continued for at least 3 months.
 - If a definite cause is found and treated, then 4 to 6 weeks of warfarin may be sufficient.
 - If no cause is found or permanent risk factors are present, it should be continued for 6 months.
 - In recurrent cases, it should be continued for longer time, even life long.
4. Rivaroxaban—It is an oral factor Xa inhibitor. Dose—15 mg 12 hourly for 21 days after food, then 20 mg for 6 months. Dose is reduced in renal failure.

N.B.: Remember about warfarin therapy:

- If INR is >3.0 but <6.0 —stop or reduce the dose.
- If INR is >6.0 but <8.0 , no bleeding—stop warfarin, restart when $INR < 5$.
- If INR is >8.0 , no bleeding or minor bleeding—stop warfarin, restart when $INR < 5$. If other factors for bleeding are present, oral Vit-k, 0.5 to 2.5 mg may be given. In major bleeding, prothrombin complex concentrate (50 U/kg) or fresh frozen plasma (15 ml/kg) may be given. Vit-k 5 mg oral or IV may be given.

Q: Why low-molecular-weight heparin is preferred?**A:** It has the following advantages:

- Does not affect APTT (no need of APTT monitoring).
- Long half-life (may be given in single dose daily).
- High bioavailability.
- Greater activity against factor Xa.
- Can be given in a fixed dose.
- Less inhibition of platelet (standard heparin can cause thrombocytopenia).

Q: What is the **mode of action** of heparin?

A: Heparin acts by potentiating the activity of antithrombin, which inhibits procoagulant enzyme activity of factors IIa, VIIa, IXa, Xa and XIa.

Q: What are the **complications** of long-term heparin use?

A: As follows:

- Osteoporosis.
- Thrombocytopenia (if heparin is used for more than 7 to 10 days).
- Hyperkalaemia (if heparin is used for more than 7 days).

Q: What is the **antidote** of heparin?

A: Protamine sulphate.

Q: What is the **mode of action** of warfarin?

A: Inhibit vitamin K-dependent factors (II, VII, IX and X).

Q: What is the **antidote** of warfarin?

A: Vitamin K.

Q: What are **thrombophlebitis** and **phlebothrombosis**?

A: Thrombophlebitis (superficial vein thrombosis): Inflammation involving superficial veins (after intravenous fluid or in varicose vein). It is characterized by:

- Pain—the main feature. Skin is inflamed with high local temperature. Prominent superficial vein, hard and tender.
- Thrombosis is attached to the vein. Hence, there is less chance of pulmonary embolism than phlebothrombosis.

Phlebothrombosis: Thrombosis in deep veins. It is characterized by:

- Pain and swelling of the leg. It is in the deeper vein, mostly asymptomatic, no inflammation.
- More chance of pulmonary embolism than thrombophlebitis.

Q: How to **prevent DVT**?

A: As follows:

- Early mobilization.
- Leg exercise.
- Elastic stockings.
- Low-dose aspirin.
- Low-molecular-weight heparin should be given following surgery or acute MI (enoxaparin 40 mg S/C daily).
- Avoid oral contraceptive pill.
- Treatment of the primary cause.

CELLULITIS

Instruction by the examiner:

- Perform the general examination of the patient.
- Examine the lower limbs. Or, look at here. What is your diagnosis?

Presentation of a Case (Supposing Left Side):

- There is erythematous and darkly pigmented area with multiple vesicles or blisters or crusts involving the dorsum of left foot extending up to the lower part of leg.
- Local temperature is raised and the part is also tender.

My diagnosis is **cellulitis**.

Q: What is **cellulitis**? What are the **causative organisms**?

A: It is the acute spreading inflammation of skin and subcutaneous tissue with local pain, swelling and erythema. It may be secondary to infection in surgery, burn or fungal infection in feet or toe. Skin on the face or lower legs (shin and ankle) are commonly affected, though cellulitis can occur in any part of the body. It appears as a swollen, red area of the skin, which is hot, tender and may spread rapidly. If left untreated, the spreading infection may rapidly turn into life threatening condition.

Causes: Commonly due to the infection by group A *Streptococcus pyogenes*, also by *Staphylococcus aureus*. In immunosuppressed or diabetic patients, Gram-negative organisms or anaerobes may be responsible.

Treatment:

- Antibiotic—phenoxymethyl penicillin, erythromycin, flucloxacillin or cephalexin.
- In severe cases—IV followed by oral therapy is given.
- In recurrent cellulitis, low dose antibiotic prophylaxis with phenoxymethylpenicillin 500 mg twice daily should be given.



Cellulitis (Right leg)



Cellulitis (Left leg)



Cellulitis (Left arm)



Cellulitis (Right hand)

Q: What **investigations** should be done in cellulitis?

A: As follows:

- CBC, ESR.
- Blood sugar.
- CRP.
- Doppler study of the lower limb vessels.

Q: What are the **differential diagnoses** of cellulitis?

A: As follows:

- DVT.
- Trauma.
- Acute arthritis.
- Ruptured Baker cyst

ERYSIPELAS

Presentation of a Case:

- Left side of the face is swollen, which is red, periorbital swelling. Local temperature is raised and the part is also tender.

My diagnosis is **erysipelas**.

Q: What is **erysipelas**? What are the **causes** and **risk factors**?

A: It is an acute, superficial form of cellulitis, which occurs classically in the cheek, but may occur in any part of the skin, caused by *Streptococcus* β -haemolyticus. Infection involves the dermis and lymphatics, is more superficial subcutaneous infection than cellulitis.

Causes: Common cause is group A streptococcus, less common are group G, C and B streptococci. Staphylococcal infection is rare.

Risk factors: Elderly, infants, children, diabetes mellitus, alcoholism, immunodeficiency, lymphatic obstruction.



Erysipelas



Erysepelas (Nose infection)

Features of erysipelas:

- Erysipelas is characterized by rapidly enlarging erythematous skin lesion, commonly involves the face, but may occur on limbs and trunk. The lesion is red, swollen, warm, indurated and painful. The margin is raised and has a sharply demarcated border (differentiating it from other skin infection).
- In severe cases, vesicles, blisters and even skin necrosis. There may be marked oedema, with eyes closed.
- LN draining the area is enlarged and tender. Occasionally, a red streak extending to the LN can be seen.
- Systemic features like high fever with chills and rigor, fatigue, arthralgia are present.
- Pustule and gangrene are usually absent. It heals without scar.

Differential diagnoses:

- Cellulitis.
- Contact dermatitis.
- Angioedema.
- Herpes zoster.

Treatment: Antibiotics—penicillin, clindamycin, erythromycin (oral or IV).

Complications:

- Septicaemia.
- Glomerulonephritis.
- Necrotizing fasciitis.
- Recurrent infection.
- Lymphatic damage.

PERIPHERAL VASCULAR DISEASE

Instruction by the examiner:

- Perform the general examination of the patient. Or examine the leg. What are your findings?

Presentation of a Case (Supposing Right Leg):

- Right leg and foot is pale, there is also wasting with prominent veins.
- Skin is shiny with loss of hairs.
- All the toes are bluish red, there is an ulcer at the tip of great toe and sole of right foot.
- Local temperature is reduced, pulse is absent in arteria dorsalis pedis and reduced in posterior tibial.
- No femoral bruit and no sensory abnormality.
- Reduced capillary return (press the nail and note the return of normal red colour, which is slow).

My diagnosis is **peripheral vascular disease**, more likely Buerger's disease (in young patient).

N.B.: If the patient is elderly, likely diagnosis is peripheral vascular disease due to atherosclerosis.

Q: Ask **one question** to the patient.

A: Smoking, with number of sticks and duration.

Q: Ask **another question**.

A: History of **intermittent claudication**. Also history of claudication distance (claudication of calf is suggestive of femoral disease and claudication of buttock is suggestive of iliac disease).

Q: What are the **differential diagnoses**?

A: As follows:

- Raynaud's disease: More in female, commonly involves the upper limb. Exposure to cold will produce typical colour change (see page 764). Buerger's disease itself can cause Raynaud's phenomenon.
- Atherosclerosis: Common in elderly. There may be bruit over femoral artery. It may be present in young, if associated with hypercholesterolaemia (look for corneal arcus, tendon xanthoma, palmar xanthoma and xanthelasma).
- Vasculitis due to other cause.
- Takayasu's disease.

Q: What are the **risk factors** for peripheral vascular disease?

A: As follows (these usually cause atherosclerosis)—

- Family history of the disease or heart attack or CVD.
- Age >50 years.
- Smoking.
- Diabetes mellitus.
- Hypertension.
- Obesity.
- Sedentary lifestyle.
- Dyslipidaemia.
- Oral contraceptive pill in female.



Raynaud's disease
(gangrene of the
tip of fingers)



Raynaud's disease
(gangrene of the
tip of fingers)



Buerger's disease
(amputation of
great toe)



Buerger's disease
(gangrene of the
tip of toes)

Q: What investigation should be done for peripheral vascular disease?

A: As follows:

- CBC, ESR.
- Blood sugar.
- CRP.
- Urine R/M/E (haematuria).
- Chest X-ray (pulmonary infiltrate is Wegener granulomatosis, PAN).
- X-ray of the involved area (may show calcification of the arteries).
- Serum lipid profile.
- Serum ANA and anti-ds-DNA.
- P-ANCA and C-ANCA,
- Doppler study of the lower limb vessels.
- Arteriography may be needed in some cases.

Q: How to treat the peripheral vascular disease?

A: As follows:

1. General measures:
 - Smoking should be stopped.
 - Reduction of weight, if obese.
 - Regular exercise.
 - Limb should be kept warm, but avoid local heat.
 - Local care of foot.
 - Use of appropriate footwear.
2. Medical treatment:
 - Treatment of any risk factors (such as control of diabetes mellitus, hypertension, dyslipidaemia).
 - Antiplatelet agent (e.g., aspirin 100 mg daily or clopidogrel 75 mg daily).
 - **Pentoxifylline—it** improves blood flow by decreasing the viscosity of blood and making red blood cells more flexible.
 - **Cilostazol—it** prevents clumping of platelets. It also dilates the blood vessels, increasing the flow of blood.
3. Surgical:
 - **Percutaneous transluminal angioplasty, stenting, endarterectomy or bypass graft.**
 - Sometimes sympathectomy may be needed.
 - Amputation may be necessary, if gangrene.

BUERGER'S DISEASE (THROMBOANGIITIS OBLITERANS)

Definition: It is an inflammatory, obliterative, arterial disease with proliferative lesion in the medium and small arteries and veins of limbs, giving rise to claudication or rest pain in fingers or toes. Superficial migratory thrombophlebitis is common. Wrist and ankle pulse are absent, but brachial and popliteal pulse are characteristically palpable. Arteriography shows narrowing or occlusion of artery below the knee, relatively healthy above the knee. It is common in young male, 20 to 40 years of age and in moderate to heavy smokers.

Bedside test in Buerger's disease:

Buerger's test: Elevate the limb at 45°, there is pallor of foot and patient may complain of pain. Then, tell the patient to sit with the feet hanging lower to the ground for 2 to 3 minutes. There is cyanotic hue (due to passage of deoxygenated blood through ischaemic tissue), followed by redness (reactive hyperaemia) in the affected foot (Buerger's sign).

N.B.: Buerger's angle is that above the horizontal plane which leads to development of pallor (<20° indicates severe ischaemia).

Treatment: As treatment of peripheral vascular disease.

BARDET–BIEDL SYNDROME

Instruction by the examiner:

- Perform the general examination of the patient.
- Look at the patient. What are your findings?



Obesity and short stature



Gynaecomastia with polydactyly (six fingers)



Polydactyly (six fingers)



Polydactyly (six toes)

Presentation of a Case:

- The patient is obese with bilateral gynaecomastia.
- There is polydactyly (one extra finger in each hand and one extra toe in each foot).

Diagnosis is **Bardet–Biedl syndrome**.

N.B.: Laurence–Moon–Biedl syndrome and Laurence–Moon–Biedl–Bardet syndrome are no longer considered synonymous. In Laurence and Moon syndrome, the patient has paraplegia, but no polydactyly or obesity, which are the main features of Bardet–Biedl syndrome.

Q: What **else** do you like to see?

A: Signs of hypogonadism and fundoscopy to see retinitis pigmentosa.

Q: What is **Bardet–Biedl syndrome**?

A: It is an autosomal recessive disorder, characterized by:

- Obesity.
- Short stature (not always).
- Mental retardation.
- Polydactyly.
- Hypogonadism (gynaecomastia and small testis are present).
- Retinitis pigmentosa.

N.B. Remember the following points:

- Hypogonadism, mental retardation and polydactyly are less frequently found in females.
- Renal structural and functional abnormalities are very common.
- Interstitial nephritis may lead to renal failure.

TONGUE

Instruction by the examiner:

- Look at the tongue? What is your finding? What is the diagnosis?

Presentation of Case No. 1 (Pale Tongue):

- The tongue is pale, smooth and shiny with atrophy of papillae.

My diagnosis is **anaemia**, which may be due to:

- Iron deficiency anaemia.
- Vitamin B₁₂ deficiency.

Presentation of Case No. 2 (Candidiasis):

- There are multiple white patches over the surface of the tongue with some denuded area at the margin.

My diagnosis is **oral candidiasis**.

Q: What are the **underlying diseases** associated with oral candidiasis?

A: As follows:

- Poor oral hygiene.
- Diabetes mellitus.
- Immunosuppressive disease, e.g., lymphoma, leukaemia, malignancy, HIV.
- Prolonged use of antibiotic, steroid and immunosuppressive drug.
- Steroid inhaler use.

Q: What is the **typical finding** in mouth in HIV?

A: Hairy leukoplakia (commonly on the lateral margin of tongue).

Q: How would you **treat** oral candidiasis?

A: As follows:

- Topical antifungal—Nystatin, econazole, miconazole.
- Systemic antifungal—Fluconazole, clotrimazole.
- Maintenance of oral hygiene, antiseptic mouthwash may be used.
- Treatment of underlying cause.

Q: What is **disseminated** candidiasis?

A: It is characterized by fever, pulmonary involvement, retinal abscess, endocarditis, skin abscess, brain abscess, osteomyelitis. Intravenous amphotericin B may be used in such cases.

Presentation of Case No. 3 (Black Tongue):

- The tongue is black and rough with pale margin.

My diagnosis is **black hairy tongue**.

Q: What are the causes?

A: Poor oral hygiene, mouth breathing, smoking, prolonged use of antibiotic, steroid, oral contraceptive pill, bismuth, radiotherapy. It is usually a benign condition.



Smooth pale tongue



Fissured tongue



Oral candidiasis



Black hairy tongue



Geographical tongue



Black tongue



Gum hypertrophy with oral candidiasis



Raw beefy tongue

READ THE FOLLOWING TOPICS IN RELATION TO TONGUE

Q: What diagnoses are possible by looking at the tongue?

A: Many diagnoses are possible by looking or examining the tongue. Such as, dry or moist, colour, size, ulceration, neoplasm. Examples are:

1. Dry or moist:

- Dry—Dehydration, mouth breathing, xerostomia (in Sjogren's syndrome), anticholinergic drug therapy.
- Moist—Sialorrhoea in post-encephalitic, Parkinsonism, local mouth infection, gastroesophageal reflux disease (GERD), heavy metal poisoning.

2. Colour:

- Pale—Anaemia.
- Yellow—Jaundice (mainly in under surface of tongue).
- Bluish—Central cyanosis. Also methaemoglobinaemia, sulphaemoglobinaemia (mainly involves the sides of the tongue), blue coloured food material.
- Bluish red—Polycythaemia.
- Black tongue (lingua nigra)—Ingestion of bismuth, liquorice, charcoal, Addison's disease (pigmented).
- Brownish—CKD.
- Magenta coloured—Riboflavin deficiency.

- Raw beefy tongue (red, swollen and painful)—Vitamin B₁₂ deficiency, niacin deficiency (pellagra).
- White patches over tongue—Candidiasis, leukoplakia, chronic superficial glossitis.
- Black hairy tongue—Smoking, fungal infection, tetracycline, penicillins.
- White or greyish coating or 'furred tongue'—Smoking, chronic debilitating disease.
- White and red strawberry tongue—Scarlet fever.
- Geographical tongue—Shows irregular red and white patches on the tongue, look like a geographic map. Slowly changing red rings and lines occur on the surface of tongue. It has no clinical significance, but may be due to riboflavin deficiency.
- Scrotal tongue (deep horizontal fissure)—No clinical significance.
- Mushroom-like tongue (sore tongue with white slough)—Corrosive poisoning.
- Blotting paper-like pallor with black pigmentation in the margin—Hook worm infestation.
- Angry looking tongue (central coating with red tip and margins)—Enteric fever.
- Glossitis or bald tongue (total loss or atrophy of papillae, smooth tongue)—Vitamin B₁₂ deficiency, iron deficiency, Coeliac disease, pellagra, tropical sprue.

3. Mass or ulcers:

- Ulcers—Aphthous, malignant, tuberculous, deformed tooth, Crohn's disease, snail track ulcer in secondary syphilis.
- Bite mark—Convulsion.
- Growth in tongue—Squamous cell carcinoma.
- Hairy leukoplakia (painless white corrugated lesion on sides)—Found in AIDS due to EBV infection.
- Papilloma (viral wart).
- Median rhomboid glossitis (lozenge shaped area with loss of papillae and fissuring in the midline of the tongue, anterior to the foramen caecum). It is a congenital anomaly.
- Cysts in the floor of the mouth—Ranula, sublingual dermoid cyst.

4. Size and shape:

- Macroglossia—Found in Down's syndrome, acromegaly, cretinism, myxoedema, primary amyloidosis, mucopolysaccharidosis (e.g., Hurler syndrome), lymphangioma, tumour infiltration.
- Microglossia (atrophy or haemiatrophy)—Found in bulbar and pseudobulbar palsy, lower motor neuron lesion of XIIth cranial nerve.
- Tongue tie (ankyloglossia)—Congenital anomaly.
- Acute swelling—Infection, angioneurotic oedema.

5. Neurological disease:

- Flaccid wasted tongue with fasciculation—Bulbar palsy.
- Spastic tongue without fasciculation—Pseudobulbar palsy.
- Jack in the box sign—Rheumatic chorea.
- Tremor—Anxiety neurosis, thyrotoxicosis, chronic alcoholism, Parkinsonism.
- Deviation of the tongue—Deviated to the opposite side is due to upper motor lesion of 12th cranial nerve. Deviated to the same side is due to lower motor lesion of 12th nerve.
- Loss of taste sensation—In anterior 2/3rd by facial nerve palsy, posterior 1/3rd by glossopharyngeal nerve lesion (Site of taste sensation—sweet at the tip, sour at the margin, bitter at the back and salty at any part of the tongue).
- Fasciculation—Bulbar palsy, LMN palsy of XIIth cranial nerve.
- Trombone tongue—Rapid forward and backward movement of the tongue, found in general paresis of insane (GPI).
- Chewing tongue—Found in athetosis.



Macroglossia



Stevens-Johnson syndrome



Oral lichen planus



Haemangioma

Q: What are the causes of mouth ulcer?

A: As follows:

- Aphthous ulcer (usually idiopathic, sometimes premenstrual).
- Trauma.
- GIT disease—Crohn's disease, ulcerative colitis, coeliac disease.
- Rheumatological disease—SLE, Behcet's syndrome, Reiter's syndrome.
- Local infection—Viral (herpes simplex), syphilis (chancre in primary and snail tract ulcer in secondary syphilis), tuberculosis, Vincent angina.
- Stevens-Johnson syndrome.
- Pemphigus vulgaris, pemphigoid.
- Erosive lichen planus.
- Cytotoxic drugs.

Q: What are the features of oral cancer?

A: As follows:

- Single irregular ulcer (without local trauma).
- Single white patch ('leukoplakia').
- Single red patch.
- Fixed mass, hard, irregular.
- Cervical lymphadenopathy.

Q: What are the causes of halitosis (bad breath)?

A: As follows:

- Poor oral hygiene.
- Foetor hepaticus (like dead mouse. It is due to methyl mercaptan, found in hepatic precoma).
- Acetone breath (present in diabetic ketoacidosis).
- Fishy ammoniacal (present in renal failure).
- Others—Smoking, alcoholism, lung abscess (foetid), bronchiectasis, Zenker diverticulum, offensive faecal smell in gastrocolic fistula.

Q: What are the causes of gum hypertrophy?

A: As follows:

- Pregnancy.
- Drug—Phenytoin, nifedipine, Cyclosporine, oral contraceptive pill with high oestrogen.
- Acute leukaemia (mainly myelomonocytic leukaemia).
- Gingivitis.
- Scurvy.

HAIRY LEUKOPLAKIA

Instruction by the examiner:

- Examine the mouth or look at the tongue. What is your diagnosis?

Presentation of a Case:

- At the margin of the tongue, there are multiple white, slightly raised, corrugated, irregular, hairy lesions with few furring.

My diagnosis is **hairy leukoplakia**.



Hairy leukoplakia



Leukoplakia

Q: What is hairy leukoplakia?

A: It is a disease characterized by irregular white patches on the side of the tongue and occasionally elsewhere on the tongue or in the mouth. It is a form of leukoplakia. Hairy leukoplakia occurs primarily in HIV-positive individuals.

Q: What is your differential diagnosis?

A: Oral candidiasis, lichen planus.

Q: What is the difference between hairy leukoplakia and oral candidiasis?

A: Oral candidiasis is usually on the surface of the tongue, can be rubbed off, respond to local and systemic antifungal therapy. Hairy leukoplakia is usually at the margin, cannot be rubbed off, does not respond to antifungals.

Q: What is the cause of hairy leukoplakia?

A: Epstein–Barr virus, usually in HIV.

Q: What is the underlying disease?

A: HIV seropositive, rare in non-HIV immunosuppressed patient. Presence of hairy leukoplakia indicates rapid progression to AIDS. It is an early finding of HIV infection.

Hairy leukoplakia has also been found in patients with Behcet syndrome and ulcerative colitis. In addition, men who are HIV positive who are smokers of more than a pack of cigarettes a day are at much greater risk of developing the condition.

Q: Can it become **malignant**?

A: No, it is not premalignant.

Q: What is the common **site** of hairy leukoplakia in tongue?

A: It usually involves the lateral border of the tongue.

Q: How to **diagnose** hairy leukoplakia?

A: Diagnosis is clinical. Biopsy is confirmatory.

Q: What is the **treatment**?

A: Zidovudine or acyclovir may be helpful. Podophyllin and retinoid may be used.

Q: What is **leukoplakia**?

A: It is defined as white patches on the mucous membranes of the mouth, often arising in response to chronic irritation. It is premalignant, may be associated with alcohol and smoking. Biopsy should always be taken. Treatment is unsatisfactory, isotretinoin may be used.

Q: What are the causes of **white patch in mouth**?

A: As follows:

- Candidiasis.
- Leukoplakia.
- Hairy leukoplakia.
- Lichen planus.
- SLE.
- Smoking.
- Poor dental hygiene.
- Aphthous ulcer.
- Squamous papilloma.
- Secondary syphilis.
- Carcinoma.
- Idiopathic keratosis.

Q: What are the **pre-malignant** oral lesions?

A: Leukoplakia, Lichen planus, Erythroplakia (red patches), Submucous fibrosis.

DUPUYTREN'S CONTRACTURE

Instruction by the examiner:

- Perform the general examination of the patient. Or examine the hand. What is your diagnosis?

Presentation of a Case:

- There is thickening of the palmar fascia, more marked along the ulnar side with flexion contracture of 4th and 5th fingers of both hands (may be all the fingers).

Q: What is your **diagnosis**? What is your **differential** diagnosis?

A: My diagnosis is **Dupuytren contracture**. My differential diagnosis is diabetic cheiroarthropathy.



Dupuytren contracture



Dupuytren contracture



Diabetic cheiroarthropathy

Q: What is **Dupuytren contracture**? What are the **causes**?

A: It is characterized by thickening, fibrosis and shortening of superficial palmar fascia, causing flexion contracture of fingers. Ring and little fingers are commonly affected. There is puckering of the skin and palpable nodules, also inability to extend the fingers. May affect the sole of foot. It is usually painless, may be bilateral, common after 40 years, but increases in with advancing age. Five times common in male than female. May be familial with dominant inheritance, common in Whites and Europeans. Mechanism is unknown, thought to be caused by local hypoxia.

Palmar fascia contains large amount of xanthine, which may be responsible.

Causes of Dupuytren contracture:

- Cirrhosis of liver (commonly alcoholic).
- Alcoholism (itself, not necessarily by cirrhosis).
- Prolonged use of antiepileptic drug (phenytoin).
- Manual worker (gardener) and chronic vibration injury.
- Traumatic.
- Familial (as autosomal dominant, associated with Garrod patch on dorsum of hand).
- Diabetes mellitus (called diabetic cheiroarthropathy, confuses with systemic sclerosis).
- Idiopathic (in many cases).
- May be associated with tuberculosis, retroperitoneal fibrosis, Peyronie's disease.

Q: How to treat Dupuytren contracture?**A:** As follows:

- Exercises, warm water application or splints may be helpful.
- If the palmar thickening is growing rapidly, triamcinolone may be injected into the growing nodule.
- Radiation therapy may be used in early stages.
- Surgery may be done in severe flexion contracture. In 50% cases, it may recur within 10 years after surgery.
- New treatment—Injection of collagenase into the scarred or fibrous tissue.

Q: What is the prognosis or natural course of Dupuytren contracture?

A: Natural course is unpredictable. It may be slowly progressive with little disability over many years. In some patients, it may progress rapidly with severe deformity and functional disability.

Q: What is diabetic cheiroarthropathy?

A: It is a complication of long-standing diabetes mellitus. In this condition, skin of the dorsum of fingers is tight, waxy, shiny and depigmented with joint stiffness and flexion deformities of many fingers. Usually painless, limitation of joint movement may be present. There is inability to extend the metacarpophalangeal (MCP) or interphalangeal (IP) joint of at least one finger bilaterally. This can be better detected by prayer sign. Occasionally, affects the wrist and shoulders. Cause of cheiroarthropathy is unknown, probably there is cross-linking and thickening of collagen. It occurs in any type of diabetes mellitus, and is confused with systemic sclerosis. There is no specific treatment.

PAGET'S DISEASE

Instruction by the examiner:

- Perform the general examination of the patient. Or look at the head or face. What is your diagnosis?

Presentation of Case No. 1 (Head And Face):

- This patient has asymmetrical enlargement of skull, more on the right, face is also enlarged more on right.

My diagnosis is **Paget's disease**.

Q: What **else** do you like to see in this patient?

A: As follows:

- Bony swelling or enlargement in other parts of the body—Leg (bowing of tibia), spine (kyphosis), other bony enlargement.
- Local warmth.
- Hearing (deafness).
- Heart (there may be evidence of high output cardiac failure).
- Fundoscopy (to see optic atrophy and angioid streaks in retina).



Asymmetrical enlargement of skull



Bowing of Right tibia

Presentation of Case No. 2 (Leg):

- There is bowing of both tibias, more on the right side.

My diagnosis is **Paget's disease**.

Q: What are the causes of **bowing of tibia**?

A: As follows:

- Congenital.
- Paget's disease.
- Rickets.
- Congenital syphilis (sabre shin).
- Fibrous dysplasia.

READ THE FOLLOWING TOPICS IN RELATION TO PAGET'S DISEASE

Q: What is **Paget's disease (osteitis deformans)**?

A: Paget's disease is characterized by excessive and disorganized resorption and formation of bone, resulting in deformity and fracture. Usually involves pelvis, femur, tibia, lumbar spines, skull and scapula. It is common after 55 years, rare before 40 years. More in temperate climate, male and female ratio is 2:3. In Paget's disease, there is increase in both osteoclastic bone resorption and osteoblastic activity. Bone formation is more than resorption. Involved bone is enlarged, deformed, weak and vascular. The disease may involve one bone (monostotic, 10 to 15%) or many bones (polyostotic).

Q: What are the causes of **Paget's disease (osteitis deformans)**?

A: Cause is unknown. Genetic factors are important. Some slow viruses like measles may be involved.

Q: What are the features of **Paget's disease**?

A: As follows:

- Many cases are asymptomatic (60 to 80%), detected incidentally during X-ray.
- There may be bone and joint pain or stiffness, bowing of the legs, deformities (in weight-bearing bones such as femur, tibia), pathological fracture, enlargement of head or other involved bones.
- Neurological features such as deafness, cranial nerve defect and nerve root pain, spinal cord compression and spinal stenosis may occur due to enlargement of affected bone.
- Warm skin over the affected bone, high output cardiac failure due to hyperdynamic circulation (due to increased vascularity of the bone).

N.B. Appearance of night pain probably indicates development of osteosarcoma in Paget's disease.

Q: What **investigations** are done in **Paget's disease**?

A: As follows:

- X-ray—Shows enlargement of bone with typical lytic and sclerotic lesion. X-ray skull shows lytic lesion, osteoporosis circumscripta, enlargement and sclerosis, thickening of trabeculae.
- Serum alkaline phosphates (high, normal in 10% cases due to monostotic involvement).
- Calcium and phosphate—Normal (calcium may be high in prolonged immobilization or fracture).
- Urinary hydroxyproline (high, it is a marker of bone breakdown).
- Isotope bone scan—most sensitive method, appear as areas of increased uptake.
- CT scan or MRI of bone may be done.
- Rarely bone biopsy.

Q: How to **treat** Paget's disease?

A: As follows:

1. For pain—NSAIDs.
2. To prevent further bone break down—
 - Bisphosphonates—Pamidronate, zoledronate, risedronate are more effective. Also etidronate and tiludronate. Hypocalcaemia may occur, so calcium and vitamin D should be given.
 - Calcitonin—Subcutaneously 100 to 200 IU, 3 times weekly for 2 to 3 months. It is less convenient and more expensive. May be given as nasal spray.
3. Orthopaedic surgery—Joint replacement or osteotomy may be needed. Neurosurgery may be needed in spinal cord compression.

Q: What are the **complications** of Paget's disease?

A: As follows:

- Bone fractures and deformities.
- Deafness due to otosclerosis of the ossicles, less due to compression of VIIIth cranial nerve.
- High output heart failure.
- Secondary osteoarthritis.
- Optic atrophy.
- Spinal cord compression causing paraplegia.
- Spinal stenosis.
- Basilar invagination (platybasia) causing brainstem sign.
- Osteosarcoma (rare but serious. Occurs in 1% in those, if the disease is >10 years).

LUPUS PERNIO

Instruction by the examiner:

- Perform the general examination of the patient. Or look at the face. What is your diagnosis?

Presentation of a Case:

- There is bluish (or violaceous) discoloration at the tip and ala of the nose.

My diagnosis is **lupus pernio**.

Q: What are the **sites** of lupus pernio?

A: Commonly in tip of nose, may be in cheeks, earlobes, hands and feet.

Q: What is the **underlying disease**?

A: It is due to sarcoidosis. It indicates chronic pulmonary sarcoidosis (may progress to fibrosis of lung). Also associated chronic uveitis, bone cyst in the phalanges may be present.

Q: What is the **differential diagnosis** of lupus pernio?

A: SLE, rosacea, rhinophyma, lupus vulgaris, leprosy.



Lupus pernio



Lupus pernio with skin rash

READ THE FOLLOWING TOPICS IN RELATION TO SARCOIDOSIS

Q: What is **sarcoidosis**? What are the **causes**?

A: It is a multisystem granulomatous disease of unknown aetiology, characterized by non-caseating granuloma in different organs. Cause is unknown. There is an imbalance between subset of T lymphocyte and disturbance of cell mediated immunity. Histologically, there is granuloma similar to TB but no caseation.

Q: What **relevants** do you want to see in sarcoidosis?

A: As follows:

- Skin lesions—erythema nodosum, plaque, maculopapular rash, hyper or hypopigmentation, subcutaneous nodule.
- Generalized lymphadenopathy (involving cervical, axillary, inguinal etc.).
- Hepatosplenomegaly.
- Lung (to see evidence of fibrosis or ILD).
- Eyes (uveitis, conjunctival nodule, lacrimal gland involvement).
- Bilateral parotid involvement.
- Neurological examination (to see evidence of neurosarcoid).

Q: What **history** should be taken in Sarcoidosis?

A: Fever, arthritis or arthralgia, cough or breathlessness.

Q: Mention one **single** investigation with the above history?

A: Chest X ray P/A view (which shows bilateral hilar lymphadenopathy).

Q: What are the **presentations** or clinical features of sarcoidosis?

A: Common in young adult, in 3rd or 4th decade, slightly more in female. Presentations may be—

1. Asymptomatic (incidental findings are—bilateral hilar lymphadenopathy in X-ray chest or abnormal liver function test).
2. Symptomatic—
 - Fever, polyarthritis or arthralgia, erythema nodosum, other skin lesions such as lupus pernio, plaque, skin rash.
 - Other features, may be present according to the involvement of the organs. There may be bilateral parotid enlargement, eye signs (episcleritis, scleritis), lacrimal gland enlargement, cardiac involvement (different types of arrhythmia, cardiomyopathy, cardiac failure), pulmonary involvement (ILD), neurological features (called neurosarcoid. There may be cranial nerve palsy, meningism, seizure, psychosis, diabetes insipidus).

N.B.: Presence of fever, arthritis or arthralgia, erythema nodosum plus BHL on x-ray is highly suggestive of sarcoidosis.

Q: What is **Lofgren's syndrome**?

A: In sarcoidosis, presence of erythema nodosum, polyarthralgia and BHL, it is called Lofgren's syndrome.

Q: What is **Heerfordt syndrome** (uveoparotid fever or Heerfordt–Waldenström syndrome)?

A: In sarcoidosis, presence of fever, bilateral parotid enlargement, anterior uveitis and lower motor neuron facial palsy is called Heerfordt syndrome.

Q: What investigation should be done in sarcoidosis?**A:** As follows:

1. CBC, ESR (shows lymphopenia, high ESR).
2. MT (negative).
3. Serum calcium and γ -globulin (usually high).
4. X-ray chest (shows BHL. May be lung infiltrate, pulmonary fibrosis, honeycomb shadow, miliary mottling, eggshell calcification).
5. X-ray of hands or feet (cyst may be found in the phalanges).
6. X-ray kidney (may show nephrocalcinosis).
7. HRCT of chest (shows ILD or DPLD).
8. Lung function tests (shows restrictive lung disease, also reduction of gas transfer).
9. Liver function tests (usually abnormal).
10. Bronchoscopy (shows cobble stone appearance of mucosa. Biopsy shows non-caseating granuloma).
11. Bronchoalveolar lavage (shows increased CD4:CD8 T-cell ratio. Increase neutrophil in pulmonary fibrosis).
12. Lung biopsy—to see ILD or DPLD. Transbronchial or percutaneous (pneumothorax may develop), open biopsy may be required (by thoracotomy).
13. FNAC or biopsy from other involved site may be needed—Lymph node, skin nodule, liver, lacrimal gland (shows non caseating granuloma).
14. Others—
 - Serum ACE (high level indicates active sarcoidosis, not helpful for diagnosis).
 - ^{67}Ga Gallium scanning of lung (shows abnormal diffuse uptake).
 - Kveim test: Intradermal injection of prepared sarcoid tissue in the forearm. In the positive case, formation of a nodule after 6 weeks. Biopsy is done from the nodule, which shows typical sarcoid lesion (**this test is not done now a days**).

Q: What are the histopathological findings in sarcoidosis?**A:** Noncaseating granuloma (shows epithelioid cells, macrophages, lymphocytes and multinucleated giant cells).**Q: How to differentiate from tuberculosis?****A:** In TB, there is caseating granuloma.**Q: What are the radiological stages of sarcoidosis?****A:** 4 stages:

- Stage 1: BHL (usually symmetrical, may be paratracheal lymphadenopathy. Spontaneous resolution occurs in 1 year).
- Stage 2: BHL with parenchymal pulmonary infiltration (often diffuse, spontaneous resolution may occur).
- Stage 3: Diffuse pulmonary infiltrate without BHL (less likely to resolve spontaneously).
- Stage 4: Pulmonary fibrosis. (The patient may complain of shortness of breath and cough. There is progressive ventilatory failure, pulmonary hypertension and cor pulmonale. Spontaneous resolution is less. X-ray chest may show eggshell calcification).

Q: Can there be sarcoidosis and tuberculosis together?**A:** Yes. In sarcoidosis, there may also be tuberculosis.

Q: How to treat sarcoidosis?**A:** As follows:

1. Acute with erythema nodosum—Bed rest with NSAID may be sufficient. If symptoms are severe, short course steroid may be given. Spontaneous resolution occurs usually.
2. If the disease is not improved 6 months after the diagnosis—prednisolone should be given, 30 mg for 6 weeks, reduced to alternate day treatment with 15 mg for 6 to 12 months.
3. Other treatment:
 - Avoid strong sunlight (may precipitate hypercalcaemia and renal impairment).
 - Topical steroid for uveitis.
 - Inhaled corticosteroid.
 - Chloroquine, hydroxychloroquine, low-dose thalidomide may be useful in cutaneous sarcoid.
 - In severe case—Methotrexate 10 to 20 mg weekly, or azathioprine 50 to 100 mg daily or TNF- α blocker (infliximab, etanercept).
 - Single lung transplantation may be done in selected case.

Q: What are the indications of steroid in sarcoidosis?**A:** As follows:

- Severe symptoms such as persistent erythema nodosum, fever, arthritis or arthralgia.
- Parenchymal lung disease in any form.
- Vital organ involvement (eye, central nervous system, heart, kidney).
- Hypercalcaemia.

Q: What is the prognosis in sarcoidosis?**A:** Mortality is 1 to 5%. Death is due to cardiac involvement, pulmonary fibrosis and cor-pulmonale or renal damage.**Q: What are the features suggestive of less favourable outlook?****A:** As follows:

- Age <40 years.
- Persistent symptoms >6 months.
- Involvement of more than three organs.
- Lupus pernio and stage 3 and 4 radiologically.
- Afro-Caribbean population.

CARDIOVASCULAR SYSTEM

2

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CARDIOVASCULAR SYSTEM

2

'The heart moves of itself and does not stop unless forever'
—Leonardo da Vinci

INTRODUCTION

In any clinical examination, a case of cardiovascular system (CVS) is frequently selected. Also, it is an extremely common system tested in any oral examination. Very often, examiner asks, 'Examine the CVS'. However, many a times, examiner may ask to perform a particular part of CVS rather than the whole system and asks questions on that particular part. For example:

- Examine the CVS.
- Examine the precordium.
- Auscultate here: 'Examiner may point a particular part', if there is obvious finding.
- Examine the pulse. What are your findings? (There may be no palpable pulse or irregular, small or high volume pulse, bradycardia, tachycardia or pulse delay etc.).
- Examine the pulse and auscultate the precordium. Describe your findings (There may be low volume, slow raising pulse. On auscultation, ejection systolic murmur may be present due to aortic stenosis).
- Palpate the precordium. What are your findings? (There may be tapping, heaving, thrusting or shifting of apex beat, diastolic or systolic thrill, palpable P2, left parasternal lift).
- What are the diseases that can be diagnosed by palpation of precordium? (See later).
- Auscultate the precordium. What are your findings? (Present systematically, starting from the heart sounds, murmur and any extra finding).

To attain a good skill, see and examine more cases. Also, make a good practice to present systematically.

Remember, the examiner may interrupt at any part of your examination and ask, 'What is your finding? What is the likely diagnosis with this finding only'?

Once you are asked to examine the CVS, more likely underlying diseases are:

- Mitral stenosis (MS).
- Mitral regurgitation (MR).
- MS with pulmonary hypertension (PH).
- MS with MR (mixed mitral valve disease).
- Aortic stenosis (AS).
- Aortic regurgitation (AR).
- AS with AR (mixed aortic valve disease).
- Congenital heart disease, such as atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), Fallot's tetralogy, dextrocardia.

EXAMINATION ROUTINE

If the examiner asks to examine CVS, then start examining systematically, including some **general examination** in relation to CVS.

Proceed as follows:

- Introduce yourself, 'Good morning, I am Dr. . . . I would like to examine you. Would you please allow me to do so? Tell me if I hurt you'.
- Position the patient should be at 45° with a backrest or pillows.
- With permission, remove the clothing to expose the chest and neck (be careful in case of a female patient).

1. Look at the patient carefully:

- Dyspnoeic or orthopnoeic (may be found in left ventricular failure), cachexia (in severe heart failure).

2. Face:

- Malar flush (in MS).
- Marfanoid face.
- Corneal arcus and xanthelasma, which may be related to atherosclerosis in ischaemic heart disease (IHD), Argyll Robertson pupil (found in AR), mouth (high arch palate in Marfan's syndrome).

3. Anaemia:

may be responsible for anaemic heart failure.

4. Cyanosis:

found in tetralogy of Fallot (TOF) and Eisenmenger's syndrome.

5. Oedema:

pitting oedema is found in congestive cardiac failure (CCF).

6. In hands:

- Clubbing.
- Koilonychia.
- Cyanosis.
- Splinter haemorrhage.
- Osler's node (red, raised, palpable, tender nodule on pulp of finger, toes, also in thenar or hypothenar area).
- Janeway lesion (non-tender, red, maculopapular lesion on palm or pulp of finger).
- Xanthoma: Palmar or tendon (related to atherosclerosis in IHD).
- Tobacco stain (found in smokers, responsible for IHD).



Clubbing



Clubbing with cyanosis



Osler's node (Finger)



Osler's Node (Toe)

Next, examine the pulse, jugular venous pressure (JVP), blood pressure (BP) and finally precordium.

PULSE:

See the following points in radial pulse:

- Rate.
- Rhythm.
- Volume (make sure you lift the arm to see collapsing pulse).
- Character.
- Condition of the vessel wall.
- Radio-femoral delay and radio-radial delay or inequality.

Compare other pulses simultaneously (carotid pulse should not be seen at the same time, may cause syncope due to cerebral ischaemia). Volume and character of pulse are better seen in brachial and carotid artery. Collapsing pulse in AR and pulsus alternans in LVF are better seen in radial.

NECK VEINS (JVP):

- The patient should be at 45°.
- Normal or engorged (internal jugular vein, lies medial to sternomastoid). If visible, see any prominent wave. See hepatojugular reflux by pressing firmly with palm over the middle of abdomen, which raises the upper limit of JVP. Next, measure the height from sternal angle (It indicates mean right atrial pressure. Normally, it is at the level of sternal angle and invisible).

Other signs in the neck:

- Tall, sinuous pulsation, oscillating up to the ear lobule (which is the prominent 'v' wave), found in tricuspid regurgitation (TR).
- Dancing carotid pulse (Corrigan's sign, found in AR).
- Vigorous arterial pulsation in neck (due to coarctation of aorta).
- Other pulsation in neck (may be present in carotid aneurysm or subclavian artery aneurysm).

BLOOD PRESSURE:

- Measure BP (normal or high). If pulse is absent in one arm or there is radio-radial or radio-femoral delay, then see B.P. in both arms. Also, in standing and lying (to see postural hypotension).
- Low systolic, normal diastolic and narrow pulse pressure (found in AS).
- High systolic, low diastolic and wide pulse pressure (found in AR).

PRECORDIUM:

INSPECTION:

- Shape of the chest and any deformity (kyphosis, scoliosis, lordosis, pectus excavatum or carinatum).
- Visible cardiac impulse (visible apex beat).
- Other impulses (such as epigastric, suprasternal, supraclavicular or any other impulse).

- Scar mark in the midline—valve replacement or coronary artery bypass grafting (CABG), thoracotomy scar (valvotomy in MS).
- Pacemaker or cardioverter defibrillator box may be seen (swelling in chest, always feel).



Midline scar in CABG



Scar of mitral valvotomy



Scar in leg for CABG



Pacemaker

PALPATION:

1. Apex beat:

- Site (localize in which intercostal space. Do not forget dextrocardia, where it is on the right side).
- Distance from midline (measure with tape).
- Nature (normal, tapping, heaving, thrusting and diffuse).

2. Thrill:

- Site (apical or basal or other intercostal space).
- Nature (systolic or diastolic or both). Feel the carotid pulse at the same time. If the thrill coincides with carotid pulse, it is systolic and if it does not coincide (comes after or before), it is diastolic.

N.B.: See both apical and basal thrill. Apical thrill is best seen by turning the patient to left lateral position with breath hold after expiration. Basal thrill is best seen by palm, the patient sitting and bending forward, breath hold after expiration. Also feel for carotid thrill.

- 3. Left parasternal heave or lift:** Place the flat of right palm in left parasternal area and feel by giving gentle sustained pressure. Presence of left parasternal heave indicates right ventricular hypertrophy (RVH).
- 4. Palpable P2** (if present, it indicates pulmonary hypertension).
- 5. Epigastric pulsation** (if present, it indicates right ventricular hypertrophy).

PERCUSSION:

Usually not done, may be helpful to diagnose pericardial effusion (area of cardiac dullness is increased) and emphysema (cardiac dullness is obliterated).

AUSCULTATION:

1. See first and second heart sounds in all areas. Feel the carotid pulse at the same time. (**Yes! Examiner notices**). **First heart sound** coincides with carotid pulse, **second sound** does not (comes after).
2. Murmur:
 - Site (mitral, tricuspid, aortic, pulmonary or parasternal area).
 - Nature: Systolic (pansystolic or ejection systolic), diastolic (mid diastolic or early diastolic) by feeling carotid pulse at the same time (systolic coincides with carotid pulse, diastolic does not).
 - Radiation (pansystolic to the left axilla, ejection systolic to the neck).
 - Relation with respiration (right sided murmur increases on inspiration, left sided murmur increases on expiration).
 - Grading of murmur (e.g., 2/6 or 4/6).
3. Added sounds (pericardial rub, opening snap).
4. Auscultate the back of chest for crepitations (pulmonary oedema).
5. Seek permission to palpate the liver (enlarged tender liver in CCF, pulsatile liver in TR) and spleen (splenomegaly in SBE).

N.B. Remember the following points:

- *If mid diastolic murmur (MDM) is present at mitral area, make sure that you have listened with Bell of stethoscope by turning the patient in left lateral position with breath hold after expiration (Yes! Examiner notices).*
- *If early diastolic murmur (EDM) is present, make sure that you have listened with the patient sitting and bending forward, breath hold after expiration.*
- *If pansystolic murmur (PSM) is present, put your stethoscope in left axilla to see radiation.*
- *If ejection systolic murmur (ESM) is present, put your stethoscope on right carotid to see radiation.*

READ THE FOLLOWING TOPICS IN RELATION TO CVS PULSE:

A. Rate: Normal rate is 60 to 90/min.

- Tachycardia: When the pulse rate is $>100/\text{min}$.
- Bradycardia: When the pulse rate is $<60/\text{min}$.

Causes of tachycardia:

- Sinus tachycardia due to any cause (see below).
- Supraventricular tachycardia.
- Atrial fibrillation (AF) and atrial flutter.
- Ventricular tachycardia.

Causes of sinus tachycardia:

1. Physiological (anxiety, emotion, exercise, pregnancy).
2. Pathological:
 - Hyperdynamic circulation (due to fever, anaemia, thyrotoxicosis, arteriovenous fistula, beriberi).

- Congestive cardiac failure (CCF).
- Myocarditis.
- Chronic constrictive pericarditis.
- Shock (except vasovagal attack).
- Acute anterior myocardial infarction (except inferior myocardial infarction, where there is bradycardia).
- Sick sinus syndrome.
- Pulmonary embolism.
- Drugs (salbutamol, atropine and other sympathomimetics).

Causes of bradycardia:

- Sinus bradycardia due to any cause (see below).
- Second-degree heart block.
- Complete heart block.
- Nodal rhythm.

Causes of sinus bradycardia:

1. Physiological (due to increased vagal tone): Athlete, during sleep.
2. Pathological:
 - Acute inferior myocardial infarction.
 - Myxoedema (due to reduction of sympathetic activity).
 - Hypothermia.
 - Raised intracranial tension (due to inhibitory effect on sympathetic outflow).
 - Obstructive jaundice (due to deposition of bilirubin in conducting system).
 - Drugs (digoxin, β -blockers, amiodarone, verapamil).

B. Rhythm: It is the interval between successive pulses. It may be regular or irregular. Irregular rhythm may be irregularly irregular or regularly irregular.

Causes of irregular pulse:

1. **Regularly irregular (2 or 3 or more normal pulse followed by drop beat). It is found in:**
 - Sinus arrhythmia (pulse increases on each inspiration, decreases on each expiration), abolished by exercise.
 - Occasional ectopics, second degree heart block (Mobitz type I, Wenckebach type).
2. **Irregularly irregular (it means irregular in rhythm and volume). Causes are:**
 - Atrial fibrillation (AF).
 - Multiple ectopics.
 - Atrial flutter with variable block.
 - Paroxysmal atrial tachycardia with variable block.

Q: How to differentiate between AF and multiple ectopics in bedside?

A: By physical exercise. With exercise, ectopics will disappear, but AF will be more prominent. Needs ECG for confirmation.

C. Volume of Pulse: It may be high or low volume.

Causes of **high volume pulse**:

- Aortic regurgitation (AR).
- Hyperdynamic circulation due to any cause.
- PDA.
- Hypertension.

Causes of **low volume pulse**:

- Shock.
- AS.
- MS.
- Chronic constrictive pericarditis.
- Pericardial effusion.
- Pulmonary hypertension (PH).

D. Character of Pulse:

- Anacrotic pulse—slow rising, small volume pulse (notch on upstroke). Found in AS.
- Plateau pulse—small volume with slow upstroke. Found in AS.
- Dicrotic pulse—When an upstroke is felt in the descending limb of the pulse wave. It is also slow rising, small volume pulse (notch on downstroke). Found in 2nd week of enteric fever.
- Bisferiens pulse—double peak of pulse, felt better in carotid (due to combination of slow rising and collapsing). Found in combined AS and AR.
- Water hammer pulse—typically found in AR (see page 161).
- Pulsus alternans—alternate strong and weak beat (Found in LVF).
- Jerky pulse—seen in carotid artery. Found in hypertrophic cardiomyopathy (HCM).
- Collapsing pulse: There is rapid upstroke and descent of pulse, seen by raising the arm above the head. Causes are: AR (common cause), hyperdynamic circulation due to any cause (see above), PDA, rupture of sinus of Valsalva, large arteriovenous communication.
- Pulsus paradoxus—When volume of pulse reduces on inspiration and increases on expiration, it is called pulsus paradoxus. It is the exaggeration of normal phenomenon (normally present in children). Better detected by sphygmomanometer. Abnormal, if >10 mmHg.

Mechanism of pulsus paradoxus: During inspiration, intrathoracic pressure falls, blood pools in pulmonary vessels and hence left heart filling is reduced with reduction of cardiac output. So, the pulse volume is low, which is reverse on expiration. Causes of pulsus paradoxus:

- Pericardial effusion (especially, cardiac tamponade).
- Chronic constrictive pericarditis.
- Acute severe asthma and chronic obstructive pulmonary disease (COPD).
- Massive pulmonary embolism.

Q: What is the difference between high volume pulse and collapsing pulse?

A: Collapsing pulse is always a high volume pulse, but all the high volume pulses are not collapsing.

JVP:

(See internal jugular vein, which lies along the medial border of sternomastoid. External jugular vein is not examined as it is tortuous and subject to compression). Normally, it is 2 cm. If >3 cm, right heart filling pressure is raised. It is a sign of right heart failure or volume overload.

Causes of raised JVP:

- CCF (right heart failure).
- Pericardial effusion.
- Chronic constrictive pericarditis.
- Pulmonary embolism.
- Tricuspid regurgitation (TR) and tricuspid stenosis (TS).
- Pulmonary regurgitation (PR) and pulmonary stenosis (PS).
- Superior vena caval obstruction (non-pulsatile).
- Others: Occasionally may occur in pregnancy, exercise, anxiety and anaemia.

Causes of prominent 'a' wave in JVP (comes just before carotid pulse):

- Pulmonary hypertension (PH).
- Pulmonary embolism.
- Tricuspid regurgitation (TR) and tricuspid stenosis (TS).
- Pulmonary stenosis (PS).

Q: What are the differences between venous pulse and arterial pulse in neck?

A: As follows:

	Venous		Arterial
1	It is wavy (two peaks with cardiac cycle)	1	Not wavy
2	It has an upper limit	2	No definite upper limit
3	Upper limit falls with inspiration	3	Not so
4	Varies with posture	4	Independent of posture
5	It is better seen than palpation	5	It is better felt than seen
6	Upper limit is increased by pressing the abdomen (hepatojugular reflux)	6	Not so
7	Just felt or lightly felt	7	Thrusting
8	Obliterated by light pressure at the root of the neck	8	Cannot be obliterated

Causes of **cannon wave** (giant 'a' wave): Occurs when atria contracts against closed tricuspid valve.

- Complete heart block ('a' wave is intermittent).
- Junctional rhythm (regular cannon wave).
- Ventricular tachycardia ('a' wave is intermittent).

Causes of **giant 'v' wave**: It is tall, sinuous, oscillating up to the ear lobule. Found in TR.

Causes of **X descent**: Chronic constrictive pericarditis and cardiac tamponade.

Cause of **slow Y descent**: Tricuspid stenosis (TS).

Cause of **rapid Y descent**: Chronic constrictive pericarditis.

Kussmaul's sign: It means raised JVP during inspiration due to reduction of right ventricular output. It is best seen with the patient at 90° with normal breathing (normally, JVP falls during inspiration). Causes are:

- Pericardial effusion (usually, cardiac tamponade).
- Chronic constrictive pericarditis.
- Right ventricular infarction.

Corrigan's sign: Dancing carotid pulse is called Corrigan's sign. Found in AR.

Carotid pulse: Prominent and forceful, found in:

- Coarctation of aorta.
- Aneurysm of aorta.
- Carotid artery aneurysm.
- Subclavian artery aneurysm.
- Others: Hyperdynamic circulation, AR and anxiety.

Precordium: Deformity of chest (kyphosis, scoliosis, pectus excavatum and pectus carinatum) may be associated with Marfan's syndrome, also may cause cor pulmonale.



Kyphosis



Scoliosis



Pectus excavatum



Pectus carinatum

Apex Beat: It is the lowermost and outermost, definitely palpable cardiac impulse. Normally, it is 9 cm from midline or 1 cm internal to the mid-clavicular line in left fifth intercostal space. Apex beat may be heaving, thrusting or tapping in nature.

- Heaving: Forceful, sustained, lifting the examining finger (pressure overload). It indicates left ventricular hypertrophy (LVH). Causes are hypertension and AS.
- Thrusting: Forceful, less sustained, lifting the examining finger (volume overload). It indicates left ventricular dilatation (found in MR and AR). Also called hyperkinetic or dyskinetic apex.
- Tapping apex: Neither sustained nor forceful, not lifting the finger. It is the palpable first heart sound. Found in MS (rarely TS).

Causes of double apex beat:

- Ventricular aneurysm.
- Hypertrophic cardiomyopathy (HCM).

Causes of impalpable apex beat:

- Thick chest wall (obesity).
- Apex is behind the rib.
- Emphysema.
- Pericardial effusion.
- Dextrocardia (apex is on the right side).

Causes of diffuse apex beat:

- Anterior myocardial infarction.
- Occasionally, in left ventricular aneurysm.

Left parasternal heave or lift: Presence of it indicates right ventricular hypertrophy (RVH).

Causes of epigastric pulsation:

- Normally palpable (in lean and thin person).
- Right ventricular hypertrophy (RVH).
- Aneurysm of abdominal aorta (expansile pulsation).
- Mass overlying aorta (carcinoma of stomach).
- Pulsatile liver (in TR).

Suprasternal pulse: Usually arterial (due to aneurysm of aorta and atherosclerosis).

Pulsation around scapula: Found in coarctation of aorta (due to anastomotic vessels).

Causes of left ventricular hypertrophy (LVH):

- Systemic hypertension.
- Aortic valvular disease (Aortic stenosis, may be aortic regurgitation).
- Mitral regurgitation.
- Coarctation of aorta.
- VSD.
- Hypertrophic cardiomyopathy.

Causes of RVH:

- Pulmonary hypertension (PH).
- Cor pulmonale.
- Pulmonary stenosis (PS).
- Pulmonary regurgitation (PR).
- Tricuspid regurgitation (TR).

HEART SOUNDS:

1. 1st heart sound:

- Loud in mitral stenosis (MS), tricuspid stenosis (TS), occasionally in anxiety, exercise.
- Soft or absent in mitral regurgitation (MR), myocarditis and cardiomyopathy.

2. 2nd heart sound: Splitting better heard in pulmonary area, in inspiration due to prolonged right ventricular systole. Causes of **wide splitting** of second sound:

- Pulmonary stenosis (PS).
- Right bundle branch block (RBBB).
- Atrial septal defect (ASD).

Cause of **wide and fixed splitting** of second sound: ASD.

Causes of **reverse splitting** of second sound (A2 is delayed):

- Left bundle branch block (LBBB).
- Aortic stenosis (AS).
- Hypertension.

Causes of **loud** second sound: Pulmonary hypertension.

Causes of **soft** second sound:

- Calcified or severe AS.
- Severe PS.
- Aortic regurgitation (AR).

Causes of **single** second sound:

- Severe aortic stenosis.
- Severe pulmonary stenosis.
- Fallot's tetralogy.

3. 3rd heart sound: It is a low pitched, distant sound due to ventricular filling, found after second sound. Better heard at the apex with the Bell of stethoscope. Causes are:

- Physiological: In young, in athlete, during pregnancy and in fever.
- Pathological: LVF, MR, anaemia, cardiomyopathy, AR. Also in chronic constrictive pericarditis (this third sound is called pericardial knock).

4. 4th heart sound: It is a low pitched sound due to atrial contraction, precedes first heart sound, better heard at the apex. Causes are:

- Due to left heart—hypertension, AS, IHD and HCM.
- Due to right heart—PS and PH.

Triple Rhythm: When in addition to first and second heart sounds, there is another sound either third or fourth, it is called triple rhythm.

Gallop Rhythm: When triple rhythm is associated with tachycardia (>100), it is called gallop rhythm. It is called 'gallop' as the cadence of sound resembles a galloping horse. Presence of gallop rhythm indicates cardiac failure (LVF). Gallop rhythm is of 3 types:

- Protodiastolic: Extra sound (third heart sound), in early or mid diastole.
- Presystolic: Extra sound (fourth heart sound) in late diastole.
- Summation: When third and fourth heart sounds coalesce, it is called summation gallop, usually with heart rate >120 /minute.

Murmur: It is a blowing sound produced by turbulent blood flow in the heart. Murmur is produced by either normal volume of blood passing through abnormal valve or increased volume of blood passing through a normal valve or congenital defect. Murmur may be:

- Systolic.
- Diastolic.
- Continuous.

Systolic murmur: 2 types—Pansystolic and Ejection systolic.

Pansystolic murmur (PSM). Causes are:

- Mitral regurgitation (MR).
- Tricuspid regurgitation (TR).
- Ventricular septal defect (VSD).
- Aortopulmonary shunt.

Ejection systolic murmur (ESM, harsh and high pitched). Causes are:

- Aortic stenosis (AS).
- Pulmonary stenosis (PS).
- Hypertrophic cardiomyopathy (HCM).
- ASD (due to increased flow through pulmonary valve).
- Other causes are due to increased flow (in pregnancy, fit athlete).

Late systolic: Found in mitral valve prolapse and also in papillary muscle dysfunction.

Diastolic murmur: 2 types—Mid diastolic murmur and Early diastolic murmur.

Causes of early diastolic murmur (EDM-soft, high pitched, blowing):

- Aortic regurgitation (AR).
- Pulmonary regurgitation (Graham Steell murmur in left second, third and fourth space).

Causes of mid diastolic murmur (MDM):

- MS.
- TS.
- Left atrial myxoma.
- Austin Flint murmur in AR.
- Carey Coomb's murmur (due to mitral valvulitis in acute rheumatic fever).
- ASD (due to increased flow through tricuspid valve).

Continuous murmur: Present in both systole and diastole. Causes are:

- PDA.
- AV fistula (coronary, pulmonary or systemic).
- Aortopulmonary fistula (may be congenital or Blalock–Taussig shunt).
- Venous hum.
- Rupture of sinus of Valsalva to right ventricle or atrium.

Innocent murmur: Benign, usually soft systolic, present in upper sternal edge (commonly pulmonary area), found in some normal people without heart problem. Not associated with thrill and grade of murmur is up to 2/6. Systolic murmur may be present also in anaemia, thyrotoxicosis and pregnancy.

Grading of Murmur:

- Grade 1/6: Very soft murmur, just audible.
- Grade 2/6: Soft.
- Grade 3/6: Moderately loud.
- Grade 4/6: Loud (thrill present).
- Grade 5/6: Very loud (thrill present).
- Grade 6/6: Very much loud, heard without placing the stethoscope over the chest (thrill present).

Thrill is present in grades 4 to 6.

Pericardial Rub:

- It is superficial, harsh, scratchy, creaking, grating, leathery sound.
- Present both in systole and diastole, louder with patient sitting, bending forward and breathing out.
- Augmented by pressing the stethoscope and also present with breath holding.
- Heard in any area of precordium, better in **bare area of heart** (part of heart not covered by the lung. This part is close to chest wall, in left lower sternum).
- Presence of pericardial rub indicates pericarditis due to any cause (such as acute MI, viral infection, uraemia and tuberculosis).

Opening Snap: It is a short, sharp, high pitched sound heard immediately after second heart sound (during diastole), produced by sudden opening of mitral valve due to raised left atrial pressure (in MS). Presence of opening snap indicates that the valve cusps are still mobile. It is absent, if the valve is calcified. Opening snap is better heard in left lower sternal edge in between mitral and tricuspid area.

Venous Hum: It is a continuous murmur due to kinking and partial obstruction of one of the large veins in the neck. It is found in the neck above the clavicle and upper part of chest, more on the right side of sternum. Venous hum can be obliterated by pressure on the neck or lying down or altering the position of neck (as there is reduction of venous obstruction). It is accentuated by sitting with head extended and turned to the side opposite to that auscultated. Venous hum has no clinical significance, commonly present in children.

Other Sounds:

- Tumour plop is found in myxoma.
- Metallic sounds are found in prosthetic metallic valve.

MITRAL STENOSIS

Instruction by the examiner:

- Palpate the pulse and examine the precordium. What are your findings?
- Palpate the precordium. What are your findings? What are the possibilities?
- Auscultate the precordium. What are your findings? What is the likely diagnosis?

Presentation of Case No. 1 (Pure Mitral Stenosis):

- Pulse: 84/min, low volume, normal in rhythm and character, no radio-radial or radio-femoral delay.
- JVP: Normal ('a' wave is prominent in pulmonary hypertension and 'a' wave is absent in atrial fibrillation).
- BP: 100/60 mmHg.

On inspection:

- Visible cardiac impulse in mitral area.

On palpation:

- Apex beat: In left fifth intercostal space, . . . cm from midline, tapping in nature.
- Thrill: Present in apical area, diastolic in nature.

On auscultation:

- 1st heart sound: Loud in all the areas, more in mitral area.
- 2nd heart sound: Normal in all areas (if pulmonary hypertension, P2 is loud in pulmonary area).
- Mid diastolic murmur (MDM) in mitral area, which is low pitched, localized, rough, rumbling (LLRR), best heard with the bell of stethoscope in left lateral position, breathing hold after expiration (mention if presystolic accentuation is present).
- Opening snap (mention, if present).

My diagnosis is **Mitral stenosis**.

*N.B.: If the murmur is not audible, ask permission that the patient should perform physical exercise. This will increase the heart rate, increase the flow across the mitral valve and murmur will be prominent. However, **exercise should be avoided** in very ill patient.*

Presentation of Case No. 2 (Mitral Stenosis with Pulmonary Hypertension):

Present as above **plus**.

- Palpable P2.
- Left parasternal heave and epigastric pulsation.
- Loud P2 on auscultation.

My diagnosis is **Mitral stenosis with pulmonary hypertension**.

Q: What are the **signs** of pulmonary hypertension?

A: As follows:

- Low volume pulse.
- Prominent 'a' wave in JVP.
- Palpable P2.
- Left parasternal heave (indicates RVH).
- Epigastric pulsation (indicates RVH).
- Loud P2 on auscultation.
- EDM (Graham Steell murmur due to pulmonary regurgitation).

Presentation of Case No. 3 (MS with Atrial Fibrillation):

- Pulse: 110/min, irregularly irregular.
- Pulsus deficit is present.
- No 'a' wave in JVP.
- No presystolic accentuation.
- Other findings are same as in case no. 1.

My diagnosis is **MS with atrial fibrillation**.

Q: What is the likely **cause** in this case?

A: Chronic rheumatic heart disease.

Q: What are the **findings**, if the patient develops CCF?

A: 3 cardinal signs of CCF are:

- Engorged and pulsatile neck veins.
- Enlarged tender liver.
- Dependent oedema.

Q: Which **disease confuses** with MS? (Or, what are the **differential** diagnoses of MS?).

A: As follows:

- Left atrial myxoma (murmur will change with posture, see below).
- Ball valve thrombus in left atrium.
- Tricuspid stenosis (TS).

Q: Why **not** this is TS?

A: In TS, MDM is prominent in left lower parasternal area, which increases during inspiration. Other features of TS are raised JVP and signs of right heart failure.

Q: Why **not** this is left atrial myxoma?

A: In left atrial myxoma, physical signs and murmur change with posture. There may be history of fever, weight loss, myalgia, arthralgia, skin rash, Raynaud's phenomenon. To confirm, echocardiography should be done.

READ THE FOLLOWING TOPICS IN RELATION TO MITRAL STENOSIS

Q: What are the **causes** of MS?

A: As follows:

1. Chronic rheumatic heart disease (commonest cause). In 50% cases, there may be history of rheumatic fever or rheumatic chorea.
2. Other causes are (very rare, do not mention unless asked): congenital, calcification of valve (usually in elderly), carcinoid syndrome.

N.B.: MS is more common in females. F:M = 2:1.

Q: What is **Lutembacher syndrome**?

A: Combination of ASD with acquired rheumatic MS (occurs in 4% cases of ASD).

Q: Why apex beat is **tapping**?

A: It is due to accentuated first heart sound.

Q: What is the **mechanism** of presystolic accentuation? **Where it is present or absent?**

A: It occurs in atrial systole, due to increased flow across the stenosed valve from left atrium to left ventricle. It is present in sinus rhythm, absent in atrial fibrillation.

Q: What is **mitral facies** or **malar flush**?

A: It is the rosy colouration of cheeks, may be bluish tinge, due to arteriovenous anastomosis and vascular stasis on the cheeks. It is not pathognomonic, may be present in normal person, also in hypothyroidism, polycythaemia.

Q: What are the **types** of MS?

A: According to severity of mitral valve area, 3 types:

- Mild: $>1.5 \text{ cm}^2$.
- Moderate: 1 to 1.5 cm^2 .
- Severe: $<1 \text{ cm}^2$.

Q: What are the **signs of severe MS**?

A: Normal area of mitral valve is 4 to 6 cm^2 . Severe, if $<1 \text{ cm}^2$. Signs of severe MS are:

- Pulse: low volume.
- 1st heart sound: soft.
- MDM: prolonged.
- Opening snap: closer to second heart sound.
- Signs of PH.
- In more severe MS, opening snap disappears and MDM quiet (due to low cardiac output).

Q: What are the **mechanisms** of pulmonary hypertension in MS?

A: As follows:

- Passive backward transmission of raised left atrial pressure.
- Reflex pulmonary arterial vasoconstriction.
- Organic obliterative change in pulmonary vascular bed.

Q: What are the complications of MS?**A:** As follows:

- Atrial fibrillation.
- Pulmonary oedema.
- PH leading to CCF.
- Pulmonary infarction.
- Systemic embolism: commonly cerebral (causing infarction with hemiplegia), also in mesenteric, renal.
- Haemoptysis.
- Ortner's syndrome (enlarged left atrium exerts pressure on left recurrent laryngeal nerve causing hoarseness of voice).
- Dysphagia due to enlarged left atrium.
- Interstitial lung disease due to prolonged pulmonary oedema.
- Chest pain in 10% cases (due to PH).
- Infective endocarditis (very rare).

Q: If this patient is unconscious, what is the likely cause?**A:** Cerebral embolism, causing cerebral infarction, usually with right sided hemiplegia. It occurs if atrial fibrillation.**Q: What is the site of lesion of cerebral infarction?****A:** Involvement of the lenticulostriate branch of left middle cerebral artery causing lesion in the internal capsule.**Q: Why syncope occurs in MS?****A:** Due to reduction of cardiac output. Also may be due to atrial fibrillation with fast ventricular rate, PH, pulmonary embolism, ball valve thrombus, cerebral embolism.**Q: What is the cause of haemoptysis in MS?****A:** Rupture of pulmonary or bronchial veins with PH (pulmonary apoplexy). May be due to pulmonary infarction.**Q: What investigations should be done in mitral stenosis?****A:** As follows:

- Chest X-ray.
- ECG: P is bifid (P-mitrale), may be RVH and RAH.
- Echocardiogram (preferably colour Doppler).
- Cardiac catheterization in some cases.
- Coronary angiogram: to exclude coronary artery disease (if associated symptoms) in some cases.

Q: How to treat MS medically?**A:** As follows:

- Restrictive activity.
- Anticoagulant to reduce the risk of embolism.
- If atrial fibrillation: digoxin, β -blocker, rate limiting calcium antagonist (e.g., verapamil, diltiazem).
- If there is CCF: diuretic, digoxin.
- Infective endocarditis is very unusual in MS. Routine prophylaxis with antibiotic is not recommended.

Q: What are the findings in chest X-ray in MS?**A:** Chest X-ray shows:

- Upper lobe veins are dilated (early feature): Upper lobe diversion (normally, ratio between upper and lower lobe veins is 1:3, which is altered to 1:1).
- Straightening of left border of heart, fullness of pulmonary conus and filling of pulmonary bay (due to enlarged left atrium).
- Kerley's B-lines (horizontal septal lines in costophrenic angle, indicates PH).
- Double shadow in right border of heart (due to enlarged left atrium).
- Widening of carina.
- Left bronchus is horizontal (due to enlarged left atrium).
- Pulmonary oedema.
- Mottling or reticulonodular shadow due to pulmonary haemosiderosis (in advanced case).
- Calcified shadow of mitral valve.

Q: What are the echocardiogram findings in MS?**A:** As follows:

- Thick mitral valve leaflet (with restricted opening), diastolic doming of anterior mitral leaflet and restricted movement of posterior mitral leaflet.
- Reduction of valvular area (narrow): Button like or funnel shaped.
- Calcification of valves (increased echogenicity).
- Shortening of chordae tendineae.
- Enlarged left atrium.
- Characteristic 'M'-shape of movement of anterior leaflet normally seen in diastole is lost and the diastolic slope (EF) is reduced.
- Thrombus may be seen.

Q: What are the indications of anticoagulant (warfarin) in MS?**A:** As follows:

- Systemic and pulmonary embolism.
- Atrial fibrillation.
- Left atrial thrombus.
- Left ventricular systolic dysfunction.

Q: What are the indications of surgery in MS?**A:** As follows:

- Symptomatic moderate or severe MS.
- Moderate or severe MS with moderate or severe MR.
- Recurrent thromboembolism.
- Episodes of pulmonary oedema without precipitating cause.
- Associated atrial fibrillation, which does not respond to medical therapy.
- PH or recurrent haemoptysis.
- Occasionally in pregnancy, with pulmonary oedema (surgery may be done in third trimester as blood volume increases significantly with increased pulmonary pressure).

Q: What **surgery** is usually done?

A: As follows:

- Valvuloplasty (percutaneous balloon mitral valvuloplasty) is the treatment of choice.
- Valvotomy—closed mitral commissurotomy (CMC, not done now a days), open mitral commissurotomy (OMC).
- Valve replacement.

Q: What are the **criteria for valvuloplasty**?

A: As follows:

- Significant symptoms.
- Pure MS.
- No or trivial MR.
- Valve: Mobile, no calcification.
- Left atrium: No thrombus.

Q: What are the **indications of valve replacement**?

A: As follows:

- Associated MR.
- If the valve is calcified and rigid.
- Thrombus in left atrium despite anticoagulation.

Q: What are the **complications of surgery**?

A: As follows:

- MR.
- Thromboembolism.
- Restenosis.

Q: What is the **contraindication of surgery in MS**?

A: Active rheumatic carditis.

Q: How to **treat MS in pregnancy**?

A: As follows:

- Bed rest.
- Correction of anaemia.
- Correction of nutrition.
- If symptomatic: Balloon valvuloplasty is the treatment of choice. If it is not possible and in severe case, can undergo successful surgery, preferably in the third trimester.
- All patients should go into full term and Caesarean section should be done.
- Advise the patient to restrict number of future pregnancy (1 to 2).

BRIEF NOTE ABOUT MYXOMA OF HEART

Definition: It is the common primary tumour of heart, usually benign, may be pedunculated, polypoid, gelatinous, attached by a pedicle to the atrial septum. It may be sporadic and familial. It occurs in any age (common in third to sixth decade) and any sex. Clinically confuses with mitral stenosis or infective endocarditis.

Sites of origin:

- Left atrium (75%), near the fossa ovalis or its margin.
- Right atrium, rarely from ventricles.

Clinical features: 3 groups of manifestations—

- Obstructive features: like MS, signs vary with posture. There is a low pitched sound called tumour plop. Syncope or vertigo may occur.
- Embolic features: systemic or pulmonary embolism.
- Constitutional features: fever, malaise, weakness, loss of weight, myalgia, arthralgia, clubbing, skin rash, Raynaud's phenomenon.

Investigations:

- CBC—anaemia, leucocytosis, polycythaemia, high ESR, thrombocytopenia or thrombocytosis.
- Chest X-ray (similar to MS).
- Echocardiogram—2D or trans-oesophageal.
- CT scan or MRI may be done.
- Hypergammaglobulinaemia.

Treatment: Surgical excision. Recurrence may occur.

N.B.: Other tumours of the heart are rhabdomyoma and sarcoma. All are rare.

MITRAL REGURGITATION

Instruction by the examiner:

- Examine the CVS. Or palpate the pulse and auscultate the precordium.
- Examine the precordium. What are your findings? What are the possibilities?
- Palpate and auscultate the precordium. What are your findings? What are the possibilities?

Presentation of a Case:

- Pulse: 80/min, normal volume, rhythm and character.
- JVP: Normal.
- BP: 120/70 mmHg.

On inspection:

- Visible cardiac impulse in mitral area.

On palpation:

- Apex beat in left . . . intercostal space, . . . cm from midline, diffuse, thrusting in character.
- Systolic thrill in left . . . intercostal space.

On auscultation:

- First heart sound: soft in mitral area, normal in other areas.
- Second heart sound: normal in all the areas (third heart sound may be present).
- There is a pan systolic murmur in mitral area, which radiates to the left axilla (reduced on inspiration and more in expiration).

My diagnosis is **Mitral regurgitation (MR)**.

Q: Can there be mid diastolic murmur in MR?

A: Yes, it may be present due to increased flow of blood through mitral valve (or if associated with MS).

Q: What are the causes of pansystolic murmur?

A: As follows:

- Mitral regurgitation (MR).
- Tricuspid regurgitation (TR).
- Ventricular septal defect (VSD).

Q: What are your differential diagnoses?

A: As follows:

- Tricuspid regurgitation (TR).
- Ventricular septal defect (VSD).

Q: Why not this is tricuspid regurgitation (TR)?

A: Because in TR, there may be-

- PSM is in left lower parasternal area.
- No radiation to axilla.
- Murmur is prominent on inspiration and less on expiration.
- Raised JVP with prominent 'V' wave.
- Liver is enlarged, tender and pulsatile.

Q: Why not VSD?**A:** Because in VSD, there may be-

- Systolic thrill in left parasternal area (fourth or fifth space).
- PSM in left parasternal area (fourth or fifth space). No radiation to axilla.

Q: What are the complications of MR?**A:** As follows:

- Acute LVE.
- Infective endocarditis.
- Systemic embolism (less than MS).
- Atrial fibrillation.
- CCF.

READ THE FOLLOWING TOPICS IN RELATION TO MITRAL REGURGITATION

Q: What are the causes of MR?**A:** As follows:

- Chronic rheumatic heart disease (rheumatic MR is more common in male).
- Mitral valve prolapse.
- Papillary muscle dysfunction (due to acute inferior myocardial infarction).
- Rupture of chordae tendineae (due to infarction, subacute bacterial endocarditis, trauma or spontaneous).
- Infective endocarditis.
- Valvotomy or valvuloplasty.
- Connective tissue diseases (Rheumatoid arthritis and SLE).
- Ankylosing spondylitis.
- Cardiomyopathy (restrictive, hypertrophic, dilated).
- Secondary to LV dilatation (hypertension, aortic valve disease).
- Associated with Marfan's syndrome, pseudoxanthoma elasticum and Ehlers–Danlos syndrome.

Q: What are the causes of acute MR?**A:** As follows:

- Trauma or surgery (valvotomy).
- SBE (due to perforation of mitral valve leaflet or chordae tendineae).
- Acute MI (due to rupture of papillary muscle).
- Acute rheumatic fever (due to mitral valvulitis).
- Spontaneous rupture of chordae tendineae or myxomatous degeneration of valve.

Q: Where does the murmur radiate following rupture of chordae tendineae?**A:** As follows:

- Rupture of anterior leaflet of chorda tendineae—murmur radiates to axilla and back.
- Rupture of posterior leaflet of chorda tendineae—murmur radiates to cardiac base and carotid arteries.

Q: What **investigations** do you suggest?

A: As follows:

- Chest X-ray (heart size is enlarged in transverse diameter).
- ECG (shows LVH).
- Echocardiogram, preferably colour Doppler.
- Cardiac catheterization, in some cases.

Q: What are the **signs** of severe MR?

A: As follows:

- Enlarged left ventricle (apex is shifted and thrusting).
- Presence of third heart sound.
- Appearance of short MDM (due to rapid filling of left ventricle).

Q: How to **treat** MR?

A: As follows:

1. Mild to moderate case, symptomatic treatment:
 - Diuretics.
 - Vasodilators (ACE inhibitor may be used).
 - Follow up every 6 months by echocardiogram.
2. Severe or progressive MR or if the ejection fraction falls to 55% and left ventricular dilatation is >60 mm, then valve replacement is needed. If papillary muscle rupture or chorda tendineae rupture in SBE, early valve replacement is suggested.
3. More recently a percutaneous mitral valve repair (MitraClip) has been used. It is appropriate in patients unsuitable for cardiac surgery.
4. Prophylactic penicillin to prevent endocarditis.

MITRAL VALVE PROLAPSE (BARLOW'S SYNDROME OR FLOPPY MITRAL VALVE)

Instruction by the examiner:

- Examine the precordium. Or palpate and auscultate the precordium.

Presentation of a Case: Present the Case as Described for MR Plus the Following:

- There is a mid systolic click and late systolic murmur (loudest at the left sternal edge).

My diagnosis is Mitral regurgitation with mitral valve prolapse (MVP).

N.B.: Cardinal signs (hallmark) of MVP are mid systolic click and late systolic murmur.

Q: What is mitral valve prolapse?

A: In this disorder, one leaflet of mitral valve (commonly posterior leaflet) prolapses into the left atrium during ventricular systole, causes MR. May be congenital anomaly or due to degenerative myxomatous changes. Also called Barlow's syndrome or floppy mitral valve. Occurs in 5 to 10% of population, more in female, F:M is 3:1.

Q: How the patient presents?

A: Mitral valve prolapse is more common in thin, young women, may be familial.

- Usually asymptomatic.
- Commonest symptom is atypical chest pain, in left submammary region, stabbing in quality.
- May be confused with anginal pain. There may be palpitation, dyspnoea, fatigue.

Q: What are the complications of mitral valve prolapse?

A: Complications are:

- Mitral regurgitation.
- Embolic stroke and TIA are rare complications.
- Infective endocarditis (rare).
- Arrhythmia (prolonged QT interval).

Q: What are the associations of mitral valve prolapse?

A: Mitral valve prolapse may be primary (common) or secondary to other diseases, such as:

- Marfan's syndrome.
- Ehlers–Danlos syndrome.
- Osteogenesis imperfecta.
- Pseudoxanthoma elasticum.
- HCM or congestive cardiomyopathy.
- Muscular dystrophy.
- ASD (20%).
- SLE.
- Anorexia nervosa.

Investigations:

- Chest X-ray.
- ECG: Non-specific ST or T wave change.
- Echocardiography.

Treatment:

- If asymptomatic: reassurance, periodic echocardiography.
- Atypical chest pain and palpitation: beta-blocker. Other antiarrhythmic drugs may be needed.
- Significant MR or AF: anticoagulation to prevent thromboembolism (aspirin may be given).
- In severe MR: mitral valve repair or replacement.
- Prophylactic penicillin to prevent infective endocarditis (specially if MR).
- Prognosis is good.

MITRAL STENOSIS WITH MITRAL REGURGITATION (MIXED MITRAL VALVE DISEASE)

Instruction by the examiner:

- Examine the CVS. Or, palpate the precordium. What are your findings? What are the possibilities?
- Palpate and auscultate the precordium. What are your findings? What are the possibilities? (In mixed valvular lesion, usual question is what is the **dominant** lesion).

Presentation of Case No. 1 (Predominant MS):

- Pulse: 88/min, low in volume, normal rhythm and character.
- JVP: Normal.
- BP: 115/60 mmHg.

On inspection:

- Visible cardiac impulse in mitral area.

On palpation:

- Apex beat: in left . . . intercostal space, . . . cm from midline, tapping in nature.
- Thrill: present in apical area, both systolic and diastolic.

On auscultation:

- First heart sound: loud in mitral area, normal in other areas.
- Second heart sound: normal in all areas.
- There is MDM in mitral area.
- There is also a PSM in mitral area, which radiates to left axilla.
- Opening snap is present (mention, if any).

My diagnosis is **Mitral stenosis with Mitral regurgitation (mixed mitral valve disease)**.

Q: What is the **predominant lesion** and why?

A: Predominant lesion is MS, because:

- Pulse: low volume.
- Apex beat: tapping in nature and not shifted.
- First heart sound: loud.

Q: What are the findings, if **MR** is predominant?

A: If MR is predominant:

- Pulse: normal volume.
- Apex beat: shifted and thrusting in nature.
- First heart sound: soft or absent.
- Third heart sound: may be present.

Q: What is the **cause** of mixed MS and MR?

A: Chronic rheumatic heart disease.

Presentation of Case No. 2 (Predominant MR):

Present as in case no. 1, except the following:

- Pulse: normal in volume.
- Apex beat: shifted and thrusting in nature.
- First heart sound: soft.
- There is also third heart sound (mention if any).

My diagnosis is **Mitral regurgitation with Mitral stenosis (mixed mitral valve disease)**.

Q: What is the **predominant** lesion and why?

A: Predominant lesion is MR (for reasons see above).

Q: What happens, if MS is predominant?

A: See above.

Q: What **investigations** do you suggest?

A: As follows:

- Chest X-ray PA view.
- ECG.
- Echocardiogram, preferably colour Doppler.
- Cardiac catheterization, in some cases.

N.B. Occasionally, difficulty arises, when the patient has loud first heart sound and apex beat is also displaced. In such cases, you should say that, 'it is difficult to be sure clinically about the dominant lesion. Echocardiogram is necessary'.

Q: **Endocarditis is common** in which lesion, MR or MS?

A: Endocarditis is common in MR.

Q: How to **treat** mixed MS and MR?

A: As follows:

1. Mild and asymptomatic:
 - Follow up is needed. Periodic echocardiography should be done.
 - Drugs—diuretic, prophylactic penicillin to prevent endocarditis.
2. In severe and symptomatic case:
 - Valve replacement is required.

AORTIC STENOSIS

Instruction by the examiner:

- Examine the precordium. Or, palpate and auscultate the precordium.
- Palpate the pulse and auscultate the precordium. What are your findings? What is the likely diagnosis?

Presentation of a Case:

- Pulse: 76/min, low volume, slow rising, normal in rhythm.
- JVP: Normal.
- BP: 90/80 mmHg (low systolic, normal diastolic and narrow pulse pressure).

On inspection:

- Visible cardiac impulse in mitral area (or nothing significant).

On palpation:

- Apex beat: in the left . . . intercostal space, . . . cm from midline, heaving in nature.
- Systolic thrill: present in aortic area, radiates to the right side of neck.

On auscultation:

- First heart sound: normal in all the areas.
- Second heart sound: A2 is soft in all areas and P2 is normal.
- There is a harsh ejection systolic murmur (ESM) in aortic area, which radiates to right side of neck.
- Reversed splitting of second heart sound, fourth heart sound may be present.

My diagnosis is **Aortic stenosis (AS)**.

Q: What are your differential diagnoses?

A: As follows:

- Pulmonary stenosis (PS).
- Hypertrophic cardiomyopathy (HCM).

Q: Why not it is PS?

A: In PS, findings are:

- Systolic thrill in pulmonary area.
- Left parasternal lift and epigastric pulsation may be present (due to RVH).
- P2 is soft, A2 is normal (wide splitting of the second heart sound may be present).
- ESM in pulmonary area, which radiates to left side of neck (murmur is more on inspiration).
- Apex is normal (not heaving as in AS).

Q: Why not it is HCM?

A: In HCM, the findings are:

- Pulse is jerky.
- Prominent 'a' wave in JVP.
- Double impulse at the apex (palpable fourth heart sound due to left atrial hypertrophy).
- Systolic thrill in left lower parasternal area.
- Family history of HCM may be present or there may be history of sudden death in family.

Q: What is the **ECG finding** in HCM?

A: ECG shows LVH and bizarre abnormalities like pseudo-infarction pattern, deep T wave inversion. Echocardiography is confirmatory.

Q: Does the **loudness** of murmur indicate severity?

A: No, prolongation of murmur indicates severity. Loudness of murmur may be associated with mild stenosis.

Q: What is the **type of pulse** in AS?

A: Plateau or anacrotic pulse which is slow rising, small volume (pulsus parvus) or late peaking (pulsus tardus).

Q: Why **anginal pain** occurs in AS?

A: There is left ventricular hypertrophy, so there is more oxygen demand. Also, there is reduced coronary flow due to less cardiac output.

READ THE FOLLOWING TOPICS IN RELATION TO AORTIC STENOSIS

Q: What are the **types** of AS?

A: 3 types:

- Valvular (involving valve cusps).
- Subvalvular (membranous diaphragm or fibrous ridge just below the aortic valve).
- Rarely, supravalvular (narrowing in ascending aorta or fibrous diaphragm just above aortic valve). It may be associated with characteristic face such as broad forehead, widely set eyes and pointed chin, mental retardation and hypercalcaemia called 'Williams syndrome'.

Q: What are the **presentations or clinical features** of aortic stenosis?

A: As follows:

- Asymptomatic in mild case.
- Breathlessness, mostly on exertion.
- Palpitation.
- Syncope during effort (due to inadequate cardiac output or reflex vasodilatation after exercise or dysrhythmia, causing cerebral hypoperfusion).
- Angina (in 50% cases with or without coronary artery disease).
- Sudden death (probably due to ventricular fibrillation).
- In elderly, may be associated with complete heart block or LBBB.

Q: What are the **complications** of aortic stenosis?

A: As follows:

- LVF.
- Infective endocarditis (10% cases).
- Sudden death due to ventricular fibrillation.
- Complete heart block (due to calcification of aortic valve).
- Systemic embolism.

Q: What are the **signs of severe AS**?

A: Signs of severe AS are:

- Pulse is low volume or absent.
- Presence of systolic thrill.
- Absent or soft A2 (or single S2).
- Harsh, loud, prolonged murmur with late peaking.
- Reversed splitting of second heart sound.
- Presence of fourth heart sound.
- Signs of pulmonary hypertension.
- Presence of heart failure or LVF (late sign).

N.B.: Also remember the following points:

- Normal area of aortic valve is 1.5 to 2 cm². It is severe, if the area is <1 cm² or valve mean pressure **gradient is >50 mmHg**.
- Critical AS: If the valve area is <0.7 cm² or valve pressure gradient is >70 mmHg.

What is **aortic sclerosis**? How to **differentiate** it from AS?

A: It is a degenerative disorder characterized by thickening of aortic valve cusps. Common in elderly, does not produce any obstruction to the outflow of blood.

Features	Aortic Stenosis	Aortic Sclerosis
1. Pulse volume	Low, slow raising	Normal
2. Apex beat	Heaving	Normal
3. Thrill	Systolic	No thrill
4. A2	Absent or soft	Normal
5. ESM	Present, radiates to the neck	Present, usually no Radiation

N.B. Risk of aortic sclerosis: may be calcification leading to AS. Risk factors like hyperlipidaemia, diabetes mellitus, smoking, hypertension which may cause aortic calcification.

Q: What are the **causes** of aortic stenosis?

A: As follows:

- Degenerative calcification in old age (commonest).
- Chronic rheumatic heart disease.
- Bicuspid aortic valve (common in young male).
- Congenital (in early age).

Cause of Aortic Stenosis According to Age:**1. Infants, children and adolescents:**

- Congenital aortic stenosis.
- Congenital subvalvular aortic stenosis.
- Congenital supralvalvular aortic stenosis.

2. Young adults to middle aged:

- Calcification and fibrosis of congenitally bicuspid aortic stenosis.

3. Middle aged to elderly:

- Senile degenerative aortic stenosis.
- Calcification of bicuspid valve.
- Rheumatic aortic stenosis.

Remember the following points in elderly patient:

- AS is the commonest form of valve disease in old age.
- It is a common cause of syncope, angina and heart failure.
- Low pulse pressure and slow rising pulse may not be present due to stiffening of the arteries.
- Surgery can be successful in the absence of co-morbidity, but operative mortality is higher. Prognosis is poor in symptomatic patient without surgery.
- Biological valve is more preferable than mechanical valves. Anticoagulant is not needed.

Q: What investigations should be done in AS?

A: As follows:

- X-ray chest (normal in early case. Enlarged left ventricle and dilated ascending aorta, calcification of valve on lateral view).
- ECG (LVH, may be LBBB, complete AV block).
- Echocardiogram, preferably colour Doppler echo.
- Cardiac catheterization (to identify associated coronary artery disease. Also, to measure the gradient between left ventricle and aorta).
- Coronary arteriography in some case: to exclude coronary artery disease.

Q: How to treat aortic stenosis?

A: As follows:

1. In mild or asymptomatic cases with valvular pressure gradient <50 mmHg:
 - Follow up (periodic echocardiogram should be done).
 - Prophylactic penicillin to prevent infective endocarditis.
2. If symptomatic or single syncopal attack:
 - Immediate valve replacement.
3. In asymptomatic patient with severe AS and deteriorating ECG:
 - Valve replacement.
4. If the patient is unfit for surgery:
 - Percutaneous valvuloplasty.
 - Transcatheter implantation with a balloon expandable stent valve is also helpful.
5. Aortic balloon valvuloplasty is useful in congenital AS. But this is of no value in old age with calcific AS (valve replacement is necessary).
6. In children, elderly or pregnancy: Valvotomy may be done. Valve replacement may be needed later.
7. Anticoagulant is necessary if associated with atrial fibrillation or mechanical valve prosthesis is used.

Q: Which prosthetic valve is **preferred** in elderly patient?

A: Biological or tissue valve is preferred than mechanical one, as biological valve does not require anticoagulation. In younger age, mechanical valve is preferred, but anticoagulant should be given.

Q: What is the **role of ETT** in AS?

A: ETT should be avoided in symptomatic patient, may be fatal. It can be done in asymptomatic case with high grade AS. ETT may be helpful in deciding the role of surgery.

Q: What are the **indications of surgery**?

A: As follows:

- All symptomatic patients (such as syncope).
- If mean systolic pressure gradient is >50 mmHg (left ventricular systolic pressure $>$ aorta).
- If the valve area is <0.7 cm² (normal: 2.5 to 3 cm²).
- Asymptomatic patient undergoing CABG, other valve disease, LV dysfunction, marked LVH.
- Progressive decline in LVEF ($<50\%$).
- Symptoms during an exercise test or drop in blood pressure.
- Ventricular tachycardia.

Q: If the patient with AS has **bleeding per rectum**, what is the likely underlying cause?

A: Angiodysplasia of the colon (Heyde's syndrome).

AORTIC REGURGITATION

Instruction by the examiner:

- Palpate the pulse and auscultate the precordium. What are your findings? What is your diagnosis?
- Examine the CVS, Or palpate and auscultate the precordium.

Presentation of a Case:

- Pulse: 92/min, high volume, collapsing type, normal in rhythm.
- JVP: Normal.
- There is dancing carotid pulse in the neck (Corrigan's sign).
- BP: 180/55 mmHg (high systolic, low diastolic and wide pulse pressure).

On inspection:

- Visible cardiac impulse (may or may not be present).

On palpation:

- Apex beat: In left . . . intercostal space, . . . cm from midline, thrusting in nature.
- Thrill: Present in left parasternal area, diastolic in nature.

On auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: A2 is absent, P2 is normal.
- There is an EDM which is high pitched, blowing, best heard in left lower parasternal area in third or fourth intercostal space, with patient bending forward and breathing hold after expiration.

N.B. Mention, if the following findings are present:

- *Ejection systolic murmur in aortic area, which radiates to right side of neck.*
- *MDM called Austin Flint murmur.*
- *Duroziez murmur (over the femoral artery).*
- *Capillary pulsation (seen in nail bed, inner side of lip, fundus during ophthalmoscopy).*

My diagnosis is **Aortic Regurgitation (AR)**.

N.B.: To diagnose AR, remember the formula of '3':

- **3 pulse:** Collapsing or water hammer, dancing carotid and capillary pulse.
- **3 BP:** High systolic, low diastolic and wide pulse pressure.
- **3 murmur:** EDM, Austin Flint murmur and Duroziez murmur.

Q: What is your **differential diagnosis**?

A: Pulmonary regurgitation (PR).

Q: In AR, what **other signs** do you like to see (if asked to examine precordium only)?

A: As follows:

- BP (see above).
- Quincke sign: Capillary pulsation at nail bed (alternate flushing and paleness of skin at the root of nail while pressure is applied at the tip of nail). May be normally present, better seen with glass slide.
- de Musset sign: Head nodding with each heart beat (with each pulse).
- Duroziez sign: Usually diastolic (may be systolic) murmur over femoral artery on gradual compression of the artery and auscultated proximally.
- Pistol shot murmur: May be heard over femoral artery (Traube sign).
- Hill sign: Higher BP in legs than arms (systolic), indicates severe AR.
- Mueller sign: Pulsation in uvula with heart beat.

N.B.: Most of the signs are rare and unhelpful.

Q: What will you look for in the **eyes and mouth** in AR?

A: As follows:

- Eye: Argyll Robertson pupil (in syphilis), dislocated lens, irregular pupils, iridodonesis (in Marfan's syndrome).
- Mouth: High arched palate (in Marfan's syndrome).
- Evidence of iritis or uveitis (in ankylosing spondylitis and rheumatoid arthritis).

Q: How to **differentiate** AR from PR?

A: In PR, findings are:

- Early diastolic murmur in pulmonary area (Graham Steel murmur), more prominent on inspiration.
- Evidence of PH may be present (e.g., palpable P2, left parasternal heave, epigastric pulsation).

N.B. PR is rare as isolated disease, usually associated with pulmonary artery dilatation due to PH, secondary to other diseases (e.g., MS).

Q: Mention one **investigation** to confirm your diagnosis.

A: Echocardiography, preferably colour Doppler.

Q: What **investigations** should be done?

A: As follows:

- X-ray chest (shows cardiomegaly, dilated ascending aorta, pulmonary oedema).
- ECG (LVH).
- Echocardiogram, preferably colour Doppler. Transoesophageal echocardiography may provide additional information about the valves and aortic root.
- Cardiac catheterization.
- Cardiac magnetic resonance and cardiac computed tomography—may be indicated for assessing the thoracic aorta in aortic dilatation or dissection. CMR can be used to quantify regurgitant volume.
- Other investigations to find out the cause according to the clinical suspicion.

Q: Why is it called **Water hammer pulse?**

A: The name was originated from a Victorian toy, 'Consisted of a sealed tube, half filled with water and half is vacuum. Inversion of the tube causes the fluid to fall rapidly without air resistance, which strike the other end with a noise like hammer blow'.

Q: What are the **causes of wide pulse pressure?**

A: As follows:

- AR.
- PDA.
- AV fistula.
- Hyperdynamic circulation (in thyrotoxicosis, anaemia, beriberi and pregnancy).

Q: What are the **causes of EDM?**

A: As follows:

- AR.
- Pulmonary regurgitation (signs of PH are present and other peripheral signs of AR are absent).

Q: Why **ESM in AR?**

A: Due to increased flow through aortic valve without AS (or may be associated with AS).

Q: Why **MDM in AR (**Austin Flint murmur**)?**

A: Due to regurgitant flow from aortic valve causing vibration of anterior leaflet of mitral valve.

Q: Why this **MDM **not** due to **MS**?**

A: In MS, there should be:

- Tapping apex beat.
- Loud first heart sound.
- MDM is associated with pre-systolic accentuation.
- Opening snap.

Q: What are the **signs of severe AR?**

A: Signs of severe AR:

- Prolonged EDM.
- A2 absent or soft.
- Presence of 3rd heart sound.
- Presence of Austin Flint murmur.
- Signs of LVF.
- Signs of pulmonary hypertension.

READ THE FOLLOWING TOPICS IN RELATION TO AORTIC REGURGITATION

Q: What are the **causes of **angina** in AR?**

A: As follows:

- Low diastolic BP, which causes reduced coronary perfusion.
- Marked compensatory LVH.

Q: What are the causes of AR?**A:** As follows:

- Chronic rheumatic heart disease.
- Infective endocarditis.
- Syphilitic aortitis.
- Bicuspid aortic valve.
- Dissecting aneurysm affecting ascending aorta.
- Hypertension (by aortic dilatation).
- Marfan's syndrome.
- Seronegative arthritis (ankylosing spondylitis, Reiter's syndrome).
- Rheumatoid arthritis.
- Cystic medial necrosis.
- Congenital.

Cause of AR according to the Site or Abnormality:**1. Due to involvement of valve:**

- Rheumatic fever.
- Infective endocarditis.
- Bicuspid aortic valve.
- Trauma.

2. Aortic root dilatation:

- Marfan's syndrome.
- Dissecting aneurysm affecting ascending aorta.
- Syphilitic aortitis.
- Hypertension.
- Trauma.
- Seronegative arthritis (ankylosing spondylitis, Reiter's syndrome, psoriatic arthropathy).
- SLE.
- Rheumatoid arthritis.
- Pseudoxanthoma elasticum.
- Osteogenesis imperfecta.

Q: What are the causes of acute AR?**A:** As follows:

- Acute bacterial endocarditis.
- Acute RF (due to valvulitis).
- Dissecting aneurysm affecting ascending aorta.
- Trauma.

Q: What are the features of acute AR?**A:** In acute AR:

- There is soft, short, early diastolic murmur with diastolic thrill.
- Most patients have heart failure.
- Peripheral signs are absent.
- No cardiomegaly.
- Patient is usually severely ill and symptomatic. It should be treated by emergency surgery.

Q: How to **differentiate** between AR of rheumatic origin and due to other causes?

A: In rheumatic origin:

- History of rheumatic fever.
- Other valvular lesion, commonly mitral.
- Echocardiogram shows thickening and shortening of cusps, fusion of commissure.

Q: What **other findings** should be looked to find out the aetiology?

A: As follows according to suspicion of cause:

- In syphilis—Argyll Robertson pupil.
- In Marfan's syndrome—dislocated lens, irregular pupils, iridodonesis, high arched palate.
- In ankylosing spondylitis—signs of iritis or uveitis, bony changes (such as lumbar lordosis, thoracic kyphosis, restricted movement of spine etc.).
- In rheumatoid arthritis—bilateral symmetrical arthropathy of small peripheral joints, also other features.
- In SLE—butterfly rash in face, other criteria of SLE (see in respective chapter).
- In bicuspid aortic valve—ejection click in early systole.

Q: How to **differentiate** syphilitic AR and rheumatic AR?

A: As follows:

Features	Syphilitic AR	Rheumatic AR
1. Age	>40 years	Early age
2. History of	Syphilis	Rheumatic fever
3. EDM	In aortic area	In left lower parasternal
4. Peripheral signs	Usually absent	Present
5. Lesion	Only AR and never AS	Both may be present
6. Echocardiogram	No cusp involvement	Cusp involvement
7. Aorta	Dilated, and calcification may occur	No calcification

N.B. Syphilis never causes AS, only aortic regurgitation.

Q: How to treat AR?**A:** As follows:

1. In asymptomatic, moderate to severe AR with normal LV function—Conservative treatment. Systolic BP should be controlled with vasodilator drugs (nifedipine or ACE inhibitors).
2. In severe case—Valve replacement.

Indications of surgery:

1. Acute severe aortic regurgitation (e.g., infective endocarditis).
2. Chronic severe aortic regurgitation with symptoms (dyspnoea, angina).
3. Asymptomatic patient with:
 - LVEF <50%.
 - LV dilatation (LV end systolic dimension >50 mm or LV end diastolic dimension >70 mm).
 - Aortic root dilatation >50 mm.
 - In those undergoing CABG or surgery of the ascending aorta or other cardiac valve.

N.B. Remember the following points:

- *Patient with chronic AR can tolerate well because of compensatory myocardial and haemodynamic adaptations. There is left ventricular enlargement and hypertrophy that causes increased stroke volume, so cardiac output is maintained.*
- *Valve should be replaced before significant left ventricular dysfunction.*
- *Both mechanical prostheses and tissue valves are used. Tissue valves are preferred in the elderly and when anticoagulants must be avoided. In young adults, mechanical valve.*
- *Antibiotic prophylaxis against infective endocarditis is not recommended.*

AORTIC STENOSIS WITH AORTIC REGURGITATION (MIXED AORTIC VALVE DISEASE)

Instruction by the examiner:

- Palpate the pulse and auscultate the precordium. What are your findings? What is your diagnosis?
- Examine the CVS, Or palpate and auscultate the precordium.

Presentation of a Case (Predominant AS) Case No. 1:

- Pulse: 100/min, low volume and slow rising, normal in rhythm, pulsus bisferiens is present (in carotid).
- JVP: Normal.
- BP: Low systolic and normal diastolic, narrow pulse pressure.

On inspection:

- Visible cardiac impulse (may or may not be).

On palpation:

- Apex beat in left . . . intercostal space, . . . cm from midline, heaving in nature.
- Systolic thrill: Present in aortic area, radiates to the right side of neck.

On auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: A2 is soft or absent and P2 is normal.
- There is ejection systolic murmur in aortic area, which radiates to the right side of neck
- Also there is EDM in the left lower parasternal area.

My diagnosis is **Aortic stenosis with Aortic regurgitation**.

Q: Which one is the **predominant** lesion and why?

A: Predominant lesion is AS, because:

- Pulse: Low volume and slow rising.
- BP: Low systolic, normal diastolic and narrow pulse pressure.
- Apex beat is heaving.
- Systolic thrill in aortic area.
- A2 is absent.

Q: What are the findings, if **AR is predominant**?

A: If AR is predominant, there will be:

- Pulse: High volume and collapsing.
- Apex beat: Shifted and thrusting.
- BP: High systolic, low diastolic and wide pulse pressure.

Q: What is your **differential** diagnosis?

A: Pulmonary stenosis with pulmonary regurgitation.

Q: What is the likely **cause** in this case?

A: Chronic rheumatic heart disease. May be congenital bicuspid aortic valve.

Q: Could it be due to **syphilis**?

A: No, syphilis never causes aortic stenosis.

Presentation of a Case (Predominant AR) Case No. 2:

Present as in case no. 1 **except:**

- Pulse: High volume and collapsing in nature.
- BP: High systolic, low diastolic and wide pulse pressure.
- Apex beat: Shifted and thrusting in nature.

My diagnosis is **Aortic regurgitation with Aortic stenosis**.

Q: Which one is **predominant** and why?

A: AR is predominant (see above).

Q: Could it be **purely** AR without stenosis?

A: Yes, ESM may be found in AR, due to increased flow through aortic valve without AS.

***N.B.:** Sometimes confusion arises regarding the predominant lesion. In such cases, colour Doppler echocardiogram should be done. Trans-oesophageal echo is also helpful. Sometimes cardiac catheterization and/or aortogram may be done.*

Q: What **investigations** do you suggest?

A: As follows:

- X-ray chest.
- ECG (LVH).
- Echocardiogram, preferably colour Doppler.
- Cardiac catheterization.
- Aortogram, in some case.

Q: How to **treat** the case?

A: As follows:

1. In mild to moderate case:
 - Follow-up.
 - Diuretic.
 - Antibiotic for SBE prophylaxis.
 - Periodic echocardiogram should be done.
2. In severe case:
 - Valve replacement.

TRICUSPID REGURGITATION (TR)

It is unusual to get pure TR. Often there is an association with other valvular lesion (e.g., MS with TR or MS and MR with TR). Whenever you get MS or MR, look carefully to find any signs of TR.

Instruction by the examiner:

- Examine the CVS. Or, palpate and auscultate the precordium.

Presentation of a Case (Pure TR):

- Pulse: 74/min, normal in volume, rhythm and character.
- JVP: Raised, there is giant 'V' wave oscillating up to ear lobule.

On inspection:

- There may be nothing significant.

On palpation:

- Apex beat: In left . . . intercostal space, . . . cm from midline, normal character.
- Thrill: Absent.
- Left parasternal lift and epigastric pulsation are present.

On auscultation:

- First heart sound: Soft in tricuspid area, normal in other areas.
- Second sound: Normal in all the areas.
- There is PSM in left lower parasternal area, no radiation and louder with inspiration (Carvallo's sign).
- MDM may be present, louder with inspiration, due to increased flow through tricuspid valve.

My diagnosis is **Tricuspid regurgitation (TR)**.

Q: What else do you want to see?

A: I want to examine the liver. May be enlarged, tender and pulsatile (occasionally ascites, oedema and pleural effusion may be present in TR).

N.B. Cardinal findings in TR:

- Prominent 'V' wave in JVP.
- PSM in left lower parasternal area, louder with inspiration (Carvallo's sign) and reduce in expiration.
- Liver: Enlarged, tender and pulsatile.

Q: What is your differential diagnosis?

A: Mitral regurgitation (MR).

Q: How to confirm your diagnosis?

A: Echocardiogram, preferably colour Doppler.

Q: What are the causes of pulsatile liver?

A: As follows:

- TR (commonest cause).
- Rarely—Arteriovenous (AV) fistula, angioma of liver, presystolic pulsation in PS.

Q: What is the **commonest** cause of TR?

A: **Functional** (secondary to dilatation of right ventricle in PH, cor pulmonale or right heart failure).

Q: What are the **causes** of TR?

A: As follows:

- **Functional**, secondary to other disease (pulmonary hypertension, cor pulmonale, right heart failure).
- **Chronic rheumatic heart disease** (usually associated with mitral or aortic valve disease).
- **Infective endocarditis (commonly involved in drug addicts).**
- Congenital heart disease (Ebstein anomaly).
- Carcinoid syndrome.
- Right ventricular papillary muscle infarction, trauma or steering wheel injury in chest.

Q: What **investigations** should be done in TR?

A: As follows:

- X-ray chest.
- ECG.
- Echocardiogram, preferably colour Doppler.
- Cardiac catheterization in some cases.

Q: What are the **differences** between TR and MR?

A: As follows:

MR	TR
1. PSM in mitral area	PSM in left lower parasternal area
2. PSM radiate to left axilla	No radiation
3. Murmur increases with expiration	Murmur increases with inspiration
4. No pulsatile liver	Pulsatile liver
5. No 'V' wave in JVP	'V' wave in JVP

Q: How to **treat** TR?

A: As follows:

1. Treatment of primary cause.
2. Drugs: diuretics, digoxin, ACE inhibitor may be given.
3. In severe organic TR:
 - **Operative repair (annuloplasty or annuloplication).**
 - Occasionally, valve replacement is needed.
4. In drug addicts with infective endocarditis of tricuspid valve:
 - **Surgical removal of the valve is done to eradicate the infection.**
 - Prosthetic valve is sometimes necessary.

Q: What is **Ebstein anomaly**?

A: It is a congenital heart disease associated with downward displacement of tricuspid valve into the right ventricle. Right atrium is large and right ventricle is small. Characteristically, multiple clicks occur due to asynchronous closure of tricuspid valve. **ASD is commonly associated with this anomaly.**

TRICUSPID STENOSIS (TS)

Instruction by the examiner:

- Examine the CVS. Or palpate and auscultate the precordium.

Presentation of a Case:

- Pulse: 70/min, normal in volume, rhythm and character.
- JVP: Raised with prominent 'a' wave (due to RAH).
- B.P.: 130/80 mmHg.

On inspection:

- Nothing significant.

On palpation:

- Apex beat: Palpable in left . . . intercostal space, . . . cm from midline, normal in character.

On auscultation:

- 1st heart sound: Normal in all the areas, soft on tricuspid area.
- 2nd heart sound: Normal in all areas.
- Mid diastolic murmur, in lower left sternal edge, louder on inspiration.
- A tricuspid opening snap may be present.

My diagnosis is **Tricuspid stenosis (TS)**.

Q: What are the **other findings** in TS?

A: Hepatomegaly, ascites and dependent oedema may be present.

Q: What is the **likely cause**?

A: Chronic rheumatic heart disease.

N.B.: Remember the following points:

- *Isolated TS is uncommon, which is found more in women than men, usually due to rheumatic heart disease, associated with mitral and/or aortic valve disease.*
- *Tricuspid stenosis is also seen in the carcinoid syndrome.*

Q: What **investigations** do you suggest?

A: As follows:

- X-ray chest (shows prominent right atrial bulge).
- ECG—peaked, tall P waves (>3 mm) in lead II (indicates right atrial enlargement).
- Echocardiogram, preferably colour Doppler.

Q: How to **treat TS**?

A: As follows:

1. Medical management:

- Diuretic.
- Salt restriction.

2. Surgery:

- Valvotomy may be done, but valve replacement is often necessary.
- Usually, other valves also need replacement because, tricuspid valve stenosis is rarely found as an isolated lesion.

PULMONARY STENOSIS (PS)

Instruction by the examiner:

- Examine the CVS. Or palpate and auscultate the precordium.

Presentation of a Case: (Usually, the Patient is an Adult or Elderly)

- Pulse: 70/min, normal in volume, rhythm and character.
- JVP: Normal (may be raised with prominent 'a' wave due to RAH).

On inspection:

- Nothing significant.

On palpation:

- Apex beat: Palpable in left . . . intercostal space, . . . cm from midline, normal in character.
- Left parasternal lift and epigastric pulsation (due to RVH).
- Systolic thrill: Present in pulmonary area.

On auscultation:

- 1st heart sound: Normal in all the areas.
- 2nd heart sound: P2 is soft in pulmonary area, A2 is normal (wide splitting of 2nd sound may be present).
- There is harsh ejection systolic murmur in pulmonary area, which radiates to the supra-sternal notch (which is louder on inspiration).
- Fourth heart sound may be present (due to right atrial contraction).
- Lung fields are clear.

My diagnosis is **Pulmonary stenosis (PS)**.

Q: What is your differential diagnosis?

A: Aortic stenosis.

Q: Why not AS?

A: In AS, findings are—

- Pulse is low volume, slow rising.
- B.P.: low systolic, normal diastolic and narrow pulse pressure.
- Apex beat heaving in nature.
- Absent or soft A2.
- Reversed splitting of 2nd heart sound.
- Harsh ejection systolic murmur in aortic area, which radiates to right side of neck.

Q: How common is PS?

A: 8 to 12% of all congenital heart disease in children. In adults, it is 15% of all congenital heart disease.

Q: What are the causes of PS?**A:** As follows:

- Congenital (commonest cause).
- Associated with Carcinoid syndrome.
- Associated with Noonan's syndrome.
- Associated with Fallot's tetralogy.
- Rarely, in chronic rheumatic heart disease.
- PS may occur, if there is rubella in pregnancy.

Q: What are the clinical features or presentations of PS?**A:** As follows:

- Usually asymptomatic.
- Symptoms such as fatigue, weakness and effort syncope may occur.
- Other features—cyanosis, features of right ventricular failure (engorged neck veins, enlarged and tender liver, dependent oedema).
- Arrhythmia (AF is commonest).

Q: What are the signs of severe PS?**A:** Signs of severe PS:

- Large 'a' wave in JVP.
- P2 is absent.
- Wide splitting of second heart sound.
- Presence of 4th heart sound.
- Murmur is prolonged, loud and harsh with late systolic peaking.
- Left parasternal lift (RVH).
- ECG shows RVH and RAH.
- Chest X-ray shows post-stenotic dilatation of pulmonary artery.

Q: What are the types of PS?**A:** 3 types:

- Valvular.
- Subvalvular (usually in Fallot's tetralogy).
- Supravalvular (usually in congenital rubella).

Q: What are the complications of PS?**A:** As follows:

- Right heart failure.
- Pulmonary embolism (no systemic).

N.B. Infective endocarditis is unusual in PS. Prophylactic antibiotic is unnecessary.

Q: How do you grade PS?**A:** As follows:

1. According to transvalvular gradient:
 - Mild: <50 mmHg.
 - Moderate: 50 to 79 mmHg.
 - Severe: >80 mmHg.
2. According to valve area:
 - Mild: >1 cm².
 - Moderate: 0.5 to 1.0 cm².
 - Severe: <0.5 cm².

Q: What investigations are done in PS?**A:** As follows:

- Chest X-ray—(shows enlarged pulmonary conus with post-stenotic dilatation, oligoemic lung fields in valvular stenosis).
- ECG.
- Echo, preferably colour Doppler.

Q: How to treat PS?**A:** As follows:

1. In mild to moderate case:
 - No specific treatment. Compatible with normal life. Follow up with regular echocardiogram.
2. In severe symptomatic case:
 - If pressure gradient is >50 mmHg—balloon valvuloplasty is the treatment of choice.
 - Percutaneous or surgical valve replacement may be necessary in some cases.

PULMONARY REGURGITATION (PR)

Instruction by the examiner:

- Examine the CVS. Or palpate and auscultate the precordium.

Presentation of a Case:

- Pulse: 70/min, normal in volume, rhythm and character.
- JVP: Normal (may be raised with prominent 'a' wave due to RAH).

On inspection:

- Nothing significant.

On palpation:

- Apex beat: Palpable in left . . . intercostal space, . . . cm from midline, normal in character.
- Palpable P2. Left parasternal lift and epigastric pulsation (due to RVH).

On auscultation:

- First heart sound: Normal in all the areas.
- 2nd heart sound: P2 is soft in pulmonary area, A2 is normal
- Early diastolic murmur in pulmonary area (Graham Steel murmur), more prominent on inspiration.
- Lung fields are clear.

N.B.: Remember the following points:

- *It is due to dilatation of the pulmonary valve ring, occurs with pulmonary hypertension (Graham Steell murmur).*
- *Usually secondary to mitral stenosis. So, look for the evidence of primary disease of heart (such as mitral stenosis).*
- *Usually causes no symptoms, treatment is rarely necessary.*

Q: What are the **causes** of PR?

A: As follows:

1. Secondary to mitral stenosis or pulmonary hypertension due to any cause.
2. Primary PR may occur in :
 - Infective endocarditis.
 - Chronic rheumatic heart disease.
 - Balloon valvuloplasty for PS.
 - Trauma due to Swan–Ganz catheterization.
 - Carcinoid syndrome.
 - Marfan's syndrome.
 - Congenital.
 - Repair of TOF.
 - Drugs—pergolide, fenfluramine.
 - Syphilis.

Q: What **investigations** are done in PS?

A: As follows:

- Chest X-ray.
- ECG.
- Echo, preferably colour Doppler.
- Cardiac catheterization.

Q: How to **treat** PS?

A: Treatment is rarely necessary. Treatment of primary cause should be done.

PROSTHETIC HEART VALVES

Instruction by the examiner:

- Examine the precordium. Or palpate and auscultate the precordium.

(**Look at the chest:** There is a vertical mid-sternal scar mark. Think of either valve replacement or CABG. In metallic valve replacement, there is metallic sound on auscultation and in tissue valve replacement, there is click).

Presentation of a case:

- Present the case starting from pulse, JVP as described before.

Add the following points:

Case No. 1 (Mitral Valve Prosthesis):

- There is a midline sternotomy scar.
- On auscultation, a metallic opening and closing sound in mitral area that coincides with first heart sound.
- Second sound is normal.

My diagnosis is **Metallic mitral valve prosthesis which appears to be functioning well.**

Q: What happens, if there is tissue valve?

A: In tissue valve prosthesis, no metallic sound or plopping sound is present. Click is present.

Case No. 2 (Aortic Valve Prosthesis):

- There is a midline sternotomy scar.
- On auscultation, metallic opening and closing sound in aortic area that coincides with second heart sound.
- First heart sound is normal.

My diagnosis is **Metallic aortic valve prosthesis which appears to be functioning well.**

Q: How to detect that the patient has prosthetic valves?

A: It is detected in the following ways:

- There is a vertical midsternal scar mark of thoracotomy.
- In metallic valve replacement, there is metallic sound on auscultation (however, modern mechanical valve, e.g., St. Jude valve makes softer opening and closing sound than older valves).
- In tissue valve prosthesis, there is no metallic sound or plopping sound. Rather, there is a click.

Q: How to detect clinically whether the replaced valve is mitral or aortic?

A: As follows:

1. Mitral valve prosthesis is detected by:

- Over the mitral valve, there is metallic sound coincides with first heart sound (sharp closing).
- Normal second heart sound.
- Diastolic flow murmur (MDM) may be present normally.
- Sharp opening or closing sound or click that coincides with the carotid pulse.

2. Aortic valve prosthesis is detected by:

- Over the aortic valve, metallic sound is present, coincides with second heart sound (sharp closing).
- Normal first heart sound. Ejection systolic murmur (ESM) may be present normally.
- Sharp opening or closing sound or click that occurs shortly after the carotid pulse.

N.B. Mostly Starr–Edwards valve is used.

Q: How to detect, if prosthetic valve is leaking?

A: As follows:

1. In mitral valve prosthesis:

- Presence of PSM indicates leaking (MDM may be normally present). Any systolic murmur of loud intensity is a sign of failure.
- Ball and cage valves project into the left ventricle, can cause a low-intensity ESM.
- Tissue valves and bileaflet valves can have a low-intensity diastolic murmur.

2. In aortic valve prosthesis:

- Presence of EDM indicates leaking (ESM may be normally present as all types of valves produce a degree of outflow obstruction).
- Tilting single disc (e.g., Bjork–Shiley) and bileaflet (e.g., St Jude) valves do not completely close and allow a regurgitant stream during diastole, so there may be low-intensity diastolic murmur. Intensity of this murmur increases as the valve fails.
- Ball and cage valves (e.g., Starr–Edwards) and tissue valves do close completely in diastole and so any diastolic murmur implies valve failure.

Q: What happens, if there is dysfunction of prosthetic valve?

A: Absence of opening and clicking or closing sounds indicates dysfunction. Unexplained heart failure may be due to dysfunction. Biological valve dysfunction is usually associated with regurgitant murmur.

Q: What are the types of prosthetic valve?

A: 2 types:

1. Metallic valves:

- Starr–Edwards valve (ball and cage valve).
- Bjork–Shiley valve (tilting disc).
- St. Jude valve (bi-leaflet, double tilting disc).

2. Tissue valves:

- Carpentier–Edwards valve.
- Hancock porcine valve.
- Ionescu–Shiley valve (less used).

N.B. Tissue valve—3 types:

- *Xenograft—Made from porcine valve or bovine pericardium. These are less durable and may require replacement after 8 to 10 years. Anticoagulation is not required.*
- *Homograft—These are cadaveric valves (aortic or pulmonary human valve). Particularly useful in young patient and in the replacement of infected valves.*
- *Autograft—Valve replacement from the same patient (i.e., pulmonary to aortic valve position).*

Q: What are the **advantages and disadvantages** of different valves?

A: As follows:

In metallic valve:

- Advantage—Incidence of valve failure is less and more durable.
- Disadvantage—Incidence of thrombosis is high, requires anticoagulant therapy. Can cause microangiopathic haemolytic anaemia.

In tissue valve:

- Advantage—Incidence of thrombosis is less, so anticoagulant therapy is not required. No haemolysis.
- Disadvantage—Incidence of valve failure is high due to stiffening and tearing of valve leaflets over 10 years. Requires repeat valve replacement and is less durable. There is degeneration and calcification in advanced stage.

Q: What are the **complications** of metallic valve?

A: As follows:

- Thromboembolism.
- Bleeding due to anticoagulation therapy.
- Microangiopathic haemolytic anaemia.
- Infective endocarditis.

Q: What are the **complications** of tissue valve?

A: As follows:

- Primary valve failure.
- Perforation or rupture.
- Degenerative changes.
- Calcification.
- Infective endocarditis.

Q: What are the **complications** of prosthetic valve?

A: As follows:

- Thromboembolism: More in metallic valve (common in mitral than aortic). Anticoagulant is necessary (INR should be between 3 and 4.5).
- Primary valve failure: Rare in metallic valve (common in tissue valve).
- Valve leaking.
- Dehiscence or detachment of valve from the site or valve ring.
- Valve obstruction by thrombosis or calcification.
- Microangiopathic haemolytic anaemia (mainly in aortic valve in 10 to 20% in 10 years).
- In tissue valve, there may be perforation, rupture and degenerative changes due to calcium deposition.
- Infective endocarditis, especially in dental procedure or catheterization. Common organism is *Staphylococcus epidermidis*. Occasionally, treatment may be difficult, may cause high mortality and may require replacing the valve again. If infection occurs within 60 days of valve replacement (early), it is mostly during surgery or contamination of intravenous cannula and if the infection occurs after 60 days (late), it is like other valve endocarditis.

Q: How to choose a particular valve?

A: In the following way:

- Young patient—if no contraindication for anticoagulant therapy, metallic valve prosthesis is preferred.
- Elderly patient or if contraindication to anticoagulant therapy, tissue valve prosthesis is preferred.

Q: If the patient has **atrial fibrillation**, which prosthesis is preferred?

A: Metallic, as anticoagulation is also needed.

Q: Which prosthesis is used in a **woman at childbearing age**?

A: Valve prosthesis in women of childbearing age is as follows:

1. **Tissue valve** is preferable in pregnancy, as no anticoagulation is necessary. However, valve degradation occurs 50% at 10 years and 90% at 15 years. Replacement of valve may be required later.
2. **Metallic valve** have excellent durability, but require lifelong anticoagulation with warfarin. Pregnancy is a hypercoagulable state due to increased levels of fibrinogen and factors VII, VIII and X, decreased levels of protein S activity, venous hypertension and stasis. So, metallic valve is not preferred. Moreover, warfarin crosses the placenta, is associated with a 5 to 12% risk of embryopathy during the first trimester. Warfarin also has an anticoagulant effect in the foetus, which may lead to spontaneous foetal intracranial haemorrhage. There is high risk for mortality and morbidity for pregnant patient with mechanical heart valves.

CONGENITAL HEART DISEASE

Common congenital heart diseases are described in this chapter. Usual cases selected in the examination are **VSD** (see page 185), **ASD** (see page 191), **PDA** (see page 194), **Fallot tetralogy** (see page 181), **coarctation of aorta** (see page 197). Others **PS** (see page 170), **TR** (see page 167) are sometimes selected; for details see the aforementioned topics on the given pages.

A BRIEF NOTE ON CONGENITAL HEART DISEASES

Any defect or malformation in one or more structures of the heart or blood vessels that occurs during pregnancy is called congenital heart disease. It affects about 1 in 100 babies. This may remain asymptomatic, or symptoms may appear after birth, at childhood or in adult.

CAUSES OF CONGENITAL HEART DISEASES:

Actual cause is unknown, but some factors may increase the risk of congenital heart disease. These are:

- Genetic abnormality (e.g., Marfan's, DiGeorge syndromes).
- Chromosomal abnormalities (e.g., Down's syndrome is associated with septal defects, mitral and tricuspid valve defects. Turner's syndrome is associated with coarctation of aorta).
- Maternal alcohol abuse is associated with septal defects.
- Maternal drug abuse or drug treatment and radiation exposure (use of thalidomide during pregnancy may be associated with amelia or paramelia).
- Maternal viral infection, such as rubella in first trimester of pregnancy is associated with PDA, pulmonary valvular and arterial stenosis, ASD.
- Maternal illness (e.g., SLE is associated with congenital complete heart block, diabetes and phenylketonuria).

TYPES OF CONGENITAL HEART DISEASES:

A. Acyanotic congenital heart diseases (communication between systemic and pulmonary circulation). 2 types:

With left-to-right shunt:

- ASD.
- VSD.
- PDA.

With no shunt:

- Coarctation of aorta.
- Bicuspid aortic valve.
- Congenital AS.
- PS or pulmonary regurgitation.
- Ebstein anomaly.
- Tricuspid valvular disease.

B. Cyanotic congenital heart diseases:

- TOF.
- Eisenmenger's syndrome (PH with right-to-left shunt).
- Transposition of great arteries.
- Others: Truncus arteriosus, tricuspid atresia, total anomalous pulmonary venous drainage.

N.B. Commonest congenital heart disease is VSD.

TETRALOGY OF FALLOT (TOF)

Instruction by the examiner:

- Look at the hands and legs. Now examine the precordium. What is the likely diagnosis?
- Examine the CVS. What are your findings?

(Look at the patient carefully. There may be gross clubbing and central cyanosis).

Presentation of a Case: (Usually a Child)

- Pulse: 80/min, normal in volume, rhythm and character.
- JVP: Normal (but absent 'a' wave).

On inspection:

- The patient may be short, dyspnoeic, cyanosed, with plethoric face.

On palpation:

- Apex beat: Palpable in left . . . intercostal space, . . . cm from midline, normal in character.
- Left parasternal lift and epigastric pulsation (due to RVH).
- Systolic thrill: Present in pulmonary area.

On auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: P2 is soft or absent in pulmonary area, A2 is normal.
- Ejection systolic murmur is present in pulmonary area, radiates to the neck, more on inspiration.

My diagnosis is **Tetralogy of Fallot (TOF)**.

Q: What is TOF?

A: It is a cyanotic congenital heart disease, which comprises of:

- Pulmonary stenosis.
- Right ventricular hypertrophy.
- VSD (perimembranous, usually large, subaortic).
- Overriding and dextroposition of aorta (aortic origin— $\frac{2}{3}$ rd from left ventricle and $\frac{1}{3}$ rd from right ventricle).

N.B.: Right ventricular outflow obstruction may be subvalvular (infundibular), valvular or supravulvular. Common obstruction is subvalvular, either alone (50%) or in combination with PS (25%).

Q: What are the possible causes associated with TOF?

A: As follows:

- Foetal hydantoin syndrome.
- Foetal carbamazepine syndrome.
- Foetal alcohol syndrome.
- Maternal phenylketonuria.
- Alagille syndrome.
- CATCH 22 malformation.

Q: Mention some **cyanotic congenital heart disease**.

A: As follows:

- TOF.
- Tricuspid atresia.
- Transposition of great vessels.
- Pulmonary atresia.
- Ebstein anomaly.

Q: What are the **cardinal features of TOF**?

A: As follows:

- Child with growth retardation.
- Clubbing and central cyanosis.
- Pulmonary ejection systolic murmur.
- History of cyanotic spells during exercise (relieved by squatting).

Q: How to assess the **severity** of TOF?

A: As follows:

- Mild case—loud and prolonged murmur.
- Severe case—reduced or no murmur.

READ THE FOLLOWING TOPICS IN RELATION TO TOF

Q: How the patient usually **presents**? Or, what are the clinical features of TOF?

A: As follows:

- Children in early age usually present with cyanotic spell (Fallot's spell) during exertion, feeding or crying. May become apnoeic and unconscious.
- In older children, Fallot's spells are uncommon but there is more cyanosis with clubbing and polycythaemia. There may be Fallot's sign.
- Shortness of breath on exertion, easy fatigability.
- Growth retardation.
- Syncope, seizure, cerebrovascular events or sudden death.

Q: What are the **precipitating factors** of cyanotic spell?

A: As follows:

- Exercise, stress.
- Fever.
- Dehydration.
- Feeding.
- Crying.
- Hypoxia.
- Acidosis.

Q: Why **syncope** occurs in TOF during exercise?

A: During exercise, there is increased pulmonary resistance and reduced systemic vascular resistance. So, there is increased right-to-left shunt and admixture of blood of right and left ventricle. As a result, there is reduced cerebral oxygenation causing syncope.

Q: Why cyanosis in TOF?

A: Because of overriding of aorta, there is admixture of blood of right and left ventricles. Cyanosis is absent in newborn or acyanotic Fallot.

Q: When cyanosis is aggravated and why?

A: Cyanosis is aggravated during exercise called cyanotic spell or Fallot's spell. It is also aggravated during feeding or crying. Cyanosis is reduced by squatting. Child may be apnoeic and unconscious. Syncope, seizure, cerebrovascular accident or sudden death may occur. Fallot's spell is uncommon in older children. Cyanotic spell is due to increased obstruction as a result of increased sympathetic stimulation that occurs during exercise, feeding and crying.

Q: How squatting relieves cyanosis?

A: During squatting position, abdominal aorta and femoral artery are compressed. There is increased arterial resistance, so increase pressure at the left ventricular level, diminished right-to-left shunt, increased flow through pulmonary artery, so reduction of admixture of right and left ventricular blood.

Q: Why no murmur of VSD in TOF?

A: Because VSD is large, so there is equal pressure in right and left ventricle.

Q: What are the complications of TOF?

A: As follows:

- Infective endocarditis (in 10% cases).
- Paradoxical emboli.
- Cerebral abscess (in 10% cases).
- Polycythaemia (due to hypoxaemia). It may cause CVA and myocardial infarction.
- Coagulation abnormality.
- Right heart failure.

Q: What investigations are done in TOF?

A: As follows:

- Chest X-ray: it shows boot-shaped heart, pulmonary conus is concave (small pulmonary artery), right ventricle is enlarged (prominent elevated apex), oligemic lung (right-sided aortic arch in 25% cases).
- Echocardiography: 2-D and colour Doppler.
- Other investigations: ECG (RVH), cardiac catheterization in some cases.
- CBC: There may be polycythaemia.

Q: How to treat TOF?

A: As follows:

- Usually total surgical correction (prior to 5 years of age): relief of the right ventricular outflow tract obstruction and closure of the VSD.
- If pulmonary artery is hypoplastic or anatomy is unfavourable: temporarily Blalock–Taussig shunt is done. Corrective surgery is done later on.

Other surgical procedures:

- Modified Blalock–Taussig shunt: tubular graft between subclavian and pulmonary artery.
- Pulmonary balloon valvuloplasty.
- Waterston shunt: Anastomosis of the back of ascending aorta to pulmonary artery. It is performed when surgery is required under the age of 3 months, because the subclavian artery is very small.
- Pott's shunt: Anastomosis of the descending aorta to back of the pulmonary artery.
- Glenn operation: Anastomosis of the SVC to the right pulmonary artery. Bidirectional Glenn procedure means anastomosis of both pulmonary arteries.

Q: What is **Blalock–Taussig shunt**?

A: It is the anastomosis between left subclavian artery and left pulmonary artery. This improves pulmonary blood flow and pulmonary artery development, and may facilitate definitive surgery later on.

Q: How to **detect Blalock–Taussig shunt** at bedside?

A: As follows:

- Thoracotomy scar.
- Left radial pulse: Absent or feeble.
- BP on the left arm: Absent or undetectable.
- Arm on the left side looks smaller than right.

N.B.: There may be a short case in the exam—‘TOF with Blalock–Taussig shunt operation’. In such case, present the case as follows:

- *Arm on the left side looks smaller than right.*
- *Thoracotomy scar.*
- *There is clubbing with central cyanosis.*
- *Left radial pulse: Absent or feeble.*
- *BP on the left arm: Absent or undetectable.*
- *There is a continuous murmur during systole and diastole in left subclavicular area, also heard posteriorly (May be confused with PDA).*

My diagnosis is **TOF with Blalock–Taussig shunt operation**.

Q: How to **treat** during cyanotic spell?

A: As follows:

- Knee–chest position of child, high concentration of O₂.
- Morphine or diamorphine injection (which relaxes right ventricular outflow obstruction).
- β -blocker.
- If medical therapy fails, emergency surgical shunt may be considered.

Prognosis is good after surgery, especially if operation is done in childhood. After surgery, restenosis, recurrence of septal defect and rhythm disorder may occur. Regular follow-up is required in every case.

- **Pentalogy of Fallot**—When TOF is associated with ASD.
- **Trilogy of Fallot**—ASD with PS with right ventricular hypertrophy.
- **Acyanotic Fallot**—When TOF is associated with infundibular PS. Outflow obstruction is mild, no cyanosis.

VENTRICULAR SEPTAL DEFECT (VSD)

Instruction by the examiner:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case:

On inspection:

- Nothing significant.

On palpation:

- Apex beat: In left . . . intercostal space, . . . cm from midline, normal in character.
- Systolic thrill: Present in left parasternal area (3rd or 4th intercostal space).

On auscultation:

- First and second heart sounds are normal in all the areas.
- PSM in left parasternal area in 3rd or 4th intercostal space, with no radiation.

My diagnosis is Ventricular septal defect (VSD).

N.B.: MDM due to increased flow through mitral valve, 3rd heart sound may be present.

Q: What are your **differential diagnoses**?

A: As follows:

- MR.
- TR.

Q: Why not this is MR?

A: In MR, findings are:

- First heart sound is soft.
- PSM in mitral area, which radiates towards the left axilla.

Q: Why not this is TR?

A: In TR, findings are:

- JVP is raised, giant 'V' wave may be present, oscillating up to the ear lobule.
- First heart sound is soft in tricuspid area.
- PSM in left lower parasternal area, no radiation, louder with inspiration.
- Liver—enlarged, tender and pulsatile.

Q: Mention **one investigation** to confirm your diagnosis.

A: Colour Doppler echocardiogram.

READ THE FOLLOWING TOPICS IN RELATION TO VSD

Q: What are the **causes** of VSD?

A: As follows:

- Commonly congenital. May be associated with Turner's syndrome, Down's syndrome or maternal rubella, maternal DM, maternal phenylketonuria, maternal alcohol consumption during pregnancy.
- Acquired—rupture of interventricular septum after acute myocardial infarction, rarely trauma (RV pacing with septal puncture, complication of alcohol septal ablation).

Q: What is the **common site** of VSD?

A: Commonly in the perimembranous part of intraventricular septum (in 90% cases).

Q: Is the **loudness** of murmur related to size of VSD?

A: Small VSD is associated with loud murmur, large defect is associated with soft murmur.

Q: What are the **types of VSD** according to site?

A: 4 types:

1. Perimembranous (Infra-cristal, conoventricular)—beneath the aortic valve.
2. Supra-cristal (conal septal, infundibular, subarterial, outlet)—below the pulmonary valve.
3. Muscular (trabecular)—occur in the muscular septum, can close spontaneously.
4. Posterior (canal type, endocardial cushion type, AV septum type, inlet)—lie posterior to the septal leaflet of tricuspid valve.

Q: What are the **types of VSD** according to the size? What are the **presentations** or clinical features?

A: 3 types according to the size:

- **Small VSD (Maladie de Roger):** Usually asymptomatic, closes spontaneously. Systolic murmur is loud and prolonged. Later, aortic regurgitation or endocarditis may occur, even after spontaneous closure.
- **Moderate VSD:** Patient presents with fatigue and dyspnoea. Heart is usually enlarged. Apex beat is shifted, systolic thrill with PSM at the left lower sternal edge.
- **Large VSD:** Murmur is soft, may lead to PH and Eisenmenger's complex may result.

Q: What are the **complications of VSD**?

A: As follows:

- Infective endocarditis (more in small VSD).
- Pulmonary hypertension with reversal of shunt (Eisenmenger's syndrome).
- Heart failure.

N.B.: When Eisenmenger's syndrome develops, there is cyanosis, clubbing with signs of PH. PSM disappears due to equalization of pressure in right and left ventricle.

Q: What **investigations** do you suggest in VSD?

A: As follows:

- ECG (shows LVH, biventricular hypertrophy).
- X-ray chest (shows cardiomegaly, large pulmonary conus, large hilar arteries, plethoric lung fields).
- Echocardiography, preferably colour Doppler.
- Cardiac catheterization may be necessary in some cases.
- CMR (cardiac magnetic resonance) angiography may be helpful.

Q: What are the **causes** of plethoric lung field?

A: ASD, VSD, PDA, also in CCF.

Q: How to **treat** VSD?

A: As follows:

1. Small VSD (with normal pulmonary artery pressure)-

- Surgery is not needed, follow up should be done.
- Spontaneous closure may occur in infants, if it is in the muscular part.
- Prophylactic penicillin for SBE.
- Reassurance and encourage normal life.

2. Moderate to large-

- Surgical correction, open or percutaneous. Percutaneous transcatheter closure may be done.
- Medical therapy—prophylaxis for SBE, diuretics.

3. When Eisenmenger syndrome develops—Surgery is contraindicated, as it aggravates right sided heart failure. Following treatments are given:

- Diuretic.
- Digoxin in some cases.
- Venesection, in polycythaemia.
- Heart–lung transplantation may be done. Mortality rate is high than heart transplantation alone.

Q: What are the **indications of surgery** in VSD?

A: As follows:

- Pulmonary to systemic flow ratio $>2:1$.
- Left ventricular dilatation.
- Left ventricular dysfunction.
- Recurrent endocarditis.
- Development of AR.
- Acute rupture of interventricular septum following acute myocardial infarction.

Q: What are the **contraindications of surgery** in VSD?

A: Development of severe irreversible pulmonary hypertension with reversal of shunt (**Eisenmenger syndrome**).

Q: What is the **impact** of pregnancy on VSD?

A: In small VSD, no problem in pregnancy. But in moderate to large VSD with pulmonary hypertension, right ventricular failure may develop. So, pregnancy should be avoided in pulmonary hypertension.

EISENMENGER'S SYNDROME

Instruction by the examiner:

- Examine the CVS.
- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case:

- Pulse: 104/min, low volume.
- JVP: Raised, with prominent 'a' wave.
- BP: 110/70 mmHg.

Precordium:

Inspection:

- Visible cardiac impulse in pulmonary area.

Palpation:

- Apex beat: In the left . . . intercostal space, . . . cm from midsternal line, normal in character.
- There is left parasternal lift, palpable P2 and epigastric pulsation.

Auscultation:

- First heart sound: Normal in all the areas.
- Second heart sound: Louder in all the areas, P2 is accentuated in pulmonary area.
- No PSM (it disappears).
- Lung fields are clear.

My diagnosis is **Eisenmenger's syndrome due to VSD**.

Q: What are your differential diagnoses?

A: As follows:

- CCF.
- Chronic cor pulmonale.

Q: Why not CCF?

A: In CCF, triad of engorged and pulsatile neck vein, enlarged tender liver and dependant oedema should be present. Usually secondary to other causes like MS or left sided heart failure, which are absent in this case.

Q: Why not chronic cor pulmonale?

A: Cor pulmonale is defined as 'right ventricular hypertrophy or enlargement with or without failure, which may be due to causes in the lungs parenchyma, pulmonary vessels or chest wall (like kyphosis, scoliosis etc.)'. All of these are absent in this case.

Q: What investigations do you suggest in this case?

A: As follows:

1. X-ray chest (shows enlargement of central pulmonary arteries with peripheral pruning of pulmonary vessels).
2. ECG (may be RVH, RAH, right axis deviation).
3. Echocardiography.
4. Cardiac catheterization in some cases.

Q: What is Eisenmenger's syndrome? What are the causes?

A: Pulmonary hypertension with reversal of shunt is called Eisenmenger's syndrome. Causes are:

- VSD.
- ASD.
- PDA.

Q: What is Eisenmenger's complex?

A: Pulmonary hypertension with reversal of shunt, when due to VSD is called Eisenmenger's complex.

Q: What is the difference between Eisenmenger's syndrome and Eisenmenger's complex?

A: Pulmonary hypertension with reversal of shunt due to any cause is called Eisenmenger's syndrome, but when due to VSD, it is called Eisenmenger's complex.

Q: What are the clinical features of Eisenmenger's syndrome?

A: As follows:

Symptoms:

- Dyspnoea.
- Fatigue.
- Syncope.
- Angina.
- Haemoptysis.
- Features of CCF.

On examination:

- Central cyanosis, not corrected by giving 100% oxygen (there may be differential cyanosis, means cyanosis in toes, not in the hand. It is found in PDA).
- Clubbing is present (there may be differential clubbing, means clubbing in toes, not in the hand. It is found in PDA).
- Pulse: Low volume.
- Prominent 'a' wave in JVP.
- Other signs of PH: Palpable P2, left parasternal lift, epigastric pulsation due to RVH. Loud P2, Ejection click and ejection systolic murmur may be present.
- TR may occur (in such case, prominent 'v' wave in JVP. Also, PSM in left lower parasternal area).
- Polycythaemia.
- Original murmur of VSD, ASD or PDA: Decreases in intensity, even may disappear.

***N.B.:** In a patient with central cyanosis, clubbing with signs of PH, likely diagnosis is Eisenmenger's syndrome.*

Q: What are the complications in Eisenmenger's syndrome?

A: As follows:

- Right heart failure.
- Thrombosis.
- Polycythaemia.
- Pulmonary embolism and infarction.
- Infective endocarditis.
- Cerebral thrombosis or abscess.
- Dysrhythmias.
- Sudden death.

Q: How to treat?**A:** As follows:

- Diuretic.
- Digoxin may be given in some cases.
- Venesection may be required, especially if polycythaemia.
- Long term intravenous epoprostenol may be tried.
- Heart lung transplantation may be done (mortality rate is very high than heart transplantation alone).
- Surgery is contraindicated in Eisenmenger's syndrome, as it aggravates right sided heart failure.

Q: What is the effect of pregnancy in Eisenmenger's syndrome?**A:** Pregnancy should be avoided. It aggravates right sided heart failure, also may be early spontaneous abortion. Mortality rate is high in mother.**Q: What happens of murmur in Eisenmenger's syndrome due to VSD, ASD or PDA?****A:** Due to reversal of shunt with pulmonary hypertension,

- In VSD—there is equalization of pressure between left and right ventricle, so the murmur disappears.
- In ASD—both MDM and ESM disappear.
- In PDA—may be only soft systolic, later on, disappears.

ATRIAL SEPTAL DEFECT (ASD)

Instruction by the examiner:

- Examine the precordium. Or, palpate and auscultate the precordium.

Presentation of a Case:

On inspection:

- Nothing significant.

On palpation:

- Apex beat: In left . . . intercostal space, . . . cm from midline, normal in character.
- Thrill: Absent.

On auscultation:

- First heart sound is normal in all the areas.
- Wide and fixed splitting of second heart sound (very important finding).
- There is ESM in left second or third intercostal spaces.
- Also MDM in tricuspid area.
- Lung fields are clear.

My diagnosis is **Atrial septal defect (ASD)**.

Q: What are your **differential diagnoses**?

A: As follows:

- PS.
- VSD.

Q: Why not this is PS?

A: In PS, the findings are:

- Soft or absent P2.
- Thrill present in pulmonary area.
- No wide and fixed splitting of second heart sound.
- ESM may radiate to the supra-sternal notch.

Q: Why not this is VSD?

A: In VSD, the findings are:

- Systolic thrill in the left lower parasternal area.
- PSM in the left lower parasternal area, no radiation to axilla.

READ THE FOLLOWING TOPICS IN RELATION TO ASD

Q: What is **wide** and **fixed** splitting of second heart sound and what is the **mechanism**?

A: Wide and fixed splitting means, it is remaining same in inspiration and expiration.

- Wide due to delay in right ventricular ejection.
- Fixed due to equal pressure in left and right atrium, so no change in 2nd heart sound with respiration (normally, wide splitting during inspiration due to delay of closure of pulmonary valve).

Q: What are the murmurs in ASD?**A:** 2 murmurs:

- ESM—due to increased flow through pulmonary valve.
- MDM—due to increased flow through tricuspid valve (it is high pitched, in MS murmur is low pitched).

*N.B.: There is no murmur due to ASD, due to equal pressure between left and right atrium.***Q: What are the ECG findings in ASD?****A:** ECG shows:

- In primum type—RBBB with left axis deviation.
- In secundum type—RBBB with right axis deviation.

Q: What are the types of ASD?**A:** Mainly 2 types:

- Ostium primum (15% cases)—due to atrioventricular defect in septum. There is involvement of AV valve, so MR or TR may develop.
- Ostium secundum (75% cases)—defect mainly at the fossa ovalis.

Other 2 types:

- Sinus venosus ASD—a) defect located at upper atrial septum near SVC (superior sinus venosus defect) or b) defect located at lower atrial septum near IVC entry point (inferior sinus venosus defect).
- Coronary sinus ASD (1%)—defect at the portion of anterior atrial septum that involves coronary sinus.

Q: What are the clinical features of ASD?**A:** As follows:

- Most are asymptomatic until adult, often detected at routine examination or with chest X-ray.
- May be weakness, fatigue, dyspnoea on exertion, chest infections.
- When PH develops—dyspnoea, haemoptysis, chest pain, cardiac failure and arrhythmias (atrial fibrillation).

*N.B.: ASD is 2 to 3 times more common in female. Ostium primum may occur in Down's syndrome.***Q: What are the complications of ASD?****A:** As follows:

- Pulmonary hypertension with reversal of shunt (Eisenmenger's syndrome).
- Arrhythmia (AF commonest).
- Embolism (pulmonary and systemic).
- Brain abscess.
- Infective endocarditis.
- Recurrent pulmonary infection.

Q: Can ASD be acquired?**A:** Iatrogenic ASD may occur during balloon mitral valvuloplasty, in which puncture of the interatrial septum is done to gain access to the left atrium from a central venous route.

Q: At what age, shunt reversal occurs? What are the **findings** in reversal of shunt?

A: Shunt reversal usually occurs after the age of 20 years. Findings in shunt reversal:

- Both murmurs reduce in intensity.
- P2 is loud.
- Systolic ejection sound is accentuated.
- Other features of PH.

Q: What is **Lutembacher syndrome**?

A: Congenital ASD with acquired rheumatic mitral stenosis.

Q: What **investigations** are done in ASD?

A: As follows:

- Chest X-ray—shows cardiomegaly (right ventricle and right atrium are enlarged, small left atrium and normal aorta), large pulmonary conus, large hilar arteries, plethoric lung fields (oligaemic lung, if PH).
- ECG (see findings above).
- Echocardiography preferably colour Doppler, but transoesophageal echo is more helpful.
- Cardiac catheterization in some cases (fluoroscopy shows hilar dance).
- CMR or CT may be helpful.

Q: How to **treat** ASD?

A: As follows:

- Small ASD: Surgery not needed, follow-up should be done (patient usually lives normal life).
- Moderate to large: Surgical closure, if the ratio of pulmonary to systemic flow is 2:1 or more.
- During catheterization, closure may be done with transcatheter clamshell device.
- In Eisenmenger's syndrome: Surgical closer is contraindicated (see in Eisenmenger's syndrome).

Q: What is the **effect** of ASD on pregnancy?

A: In uncomplicated ASD, pregnancy is well tolerated. But in Eisenmenger's syndrome, pregnancy should be avoided, because of high maternal and foetal mortality.

PATENT DUCTUS ARTERIOSUS (PDA)

Instruction by the examiner:

- Examine the CVS. Or palpate the pulse and examine the precordium.

Presentation of a Case:

- Pulse: 80/min, high volume or collapsing, normal in rhythm.
- JVP: Normal.
- BP: 130/60 mmHg (wide pulse pressure).

On inspection:

- Visible cardiac impulse in apical area and another impulse in pulmonary area.

On palpation:

- Apex beat: In left . . . intercostal space, . . . cm from midline, thrusting or heaving in nature.
- Systolic thrill: Present in pulmonary area (may be diastolic also).
- Pulmonary arterial pulsation may be felt.

On auscultation:

- 1st and 2nd heart sounds are normal in all areas.
- There may be reverse splitting of 2nd heart sound, if large shunt.
- There is a continuous murmur in left 2nd and 3rd intercostal space, more prominent in systole (murmur is prominent on expiration, may be heard posteriorly) and radiates to the neck.
- May be a MDM (due to increased flow).
- Lung fields are clear.

My diagnosis is **Patent Ductus Arteriosus (PDA)**.

N.B.: During foetal life, ductus arteriosus connects pulmonary artery at its bifurcation to the descending aorta just below the origin of left subclavian artery and permits blood flow from pulmonary artery to aorta. After birth, within hours or days, it closes spontaneously and remains as ligamentum arteriosum. In some cases (particularly in premature babies and maternal rubella), the ductus persists. In PDA, it allows blood to flow from aorta to pulmonary artery. Up to 50% of left ventricular output may enter into pulmonary artery, because pressure in aorta is higher.

Q: What are your **differential diagnoses?**

A: Typical continuous murmur is highly suggestive of PDA. However, any cause of continuous murmur should be excluded such as:

- Arteriovenous fistula (coronary, pulmonary or systemic).
- Venous hum.
- Rupture of sinus of Valsalva to the right ventricle or atrium.

Q: What is venous hum?

A: It is a continuous murmur due to kinking and partial obstruction of one of the large veins in the neck. It is found in the neck above the clavicle and upper part of chest, more on the right side of sternum. Hum can be obliterated by pressure on the neck or lying down or altering the position of neck (due to reduction of venous obstruction). It is accentuated by sitting with head extended and turned to the side opposite to that auscultated. Venous hum has no clinical significance, commonly present in children, should not be confused with any pathology.

READ THE FOLLOWING TOPICS IN RELATION TO PDA

Q: What is the murmur in PDA?

A: Continuous murmur (machinery murmur like **train in a tunnel**), with late systolic accentuation.

Q: What are the causes of continuous murmur?

A: As follows:

- PDA.
- Arteriovenous fistula (coronary, pulmonary or systemic).
- Aortopulmonary fistula (may be congenital or Blalock–Taussig shunt).
- Venous hum.
- Rupture of sinus of Valsalva to the right ventricle or atrium.

Q: What are the causes of PDA?

A: Common in females. M:F ratio is 1:3. Probable causes are:

- Maternal rubella in the first trimester.
- Birth at high altitude with continuous prenatal hypoxia.
- Prematurity.
- Others—Maternal hypoxia, Foetal alcohol syndrome, Maternal amphetamine, phenytoin use.

Q: What are the clinical features of PDA?

A: As follows:

- Most are asymptomatic until adult, often detected at routine examination.
- If duct is large—there may be dyspnoea, growth and development retardation.
- When PH develops—dyspnoea, haemoptysis, chest pain, cardiac failure and arrhythmias.

Q: What are the findings in reversal of shunt?

A: As follows:

- Cyanosis and clubbing in lower limbs, absent in upper limbs (differential cyanosis and clubbing).
- Murmur is quiet or absent or systolic only (diastolic is absent).
- Evidence of PH.

Q: What are the complications of PDA?

A: As follows:

- Pulmonary hypertension with reversal of shunt (Eisenmenger's syndrome).
- Congestive cardiac failure (CCF).
- Infective endocarditis.
- Arrhythmia (AF).
- Ductal aneurysm, rupture or calcification.

Q: What investigations should be done in PDA?**A:** As follows:

- ECG (may be normal or LVH and RVH in Eisenmenger's syndrome).
- Chest X-ray: Shows cardiomegaly (left ventricle and left atrium are enlarged, also large aorta), large pulmonary conus, large hilar arteries, lung fields are plethoric.
- Echocardiography: 2-D and colour Doppler.
- Cardiac catheterization may be necessary in some cases.
- Angiography may be done.
- CMR may be helpful.

Q: How to treat PDA?**A:** As follows:

- If small PDA: can be closed at cardiac catheterization using percutaneously delivered device.
- If large PDA: surgical closure.
- Prophylaxis for infective endocarditis.
- In neonate, indomethacin (0.2 mg/kg IV) or ibuprofen may be given, which can close PDA (by inhibiting prostaglandin E synthesis. Prior to birth, duct is kept patent by the effect of circulating prostaglandin). It is effective, if given in the first 14 days of life, not helpful in older children.
- If Eisenmenger's syndrome develops, surgery is contraindicated (see in Eisenmenger's syndrome).

Q: What is the prognosis in untreated case?**A:** Mortality rate is:

- 20% by the age of 20 years.
- 42% by the age of 45 years.
- 60% by the age of 60 years.

Q: What are the causes of death in PDA?**A:** If untreated, heart failure, PH or endocarditis.

COARCTATION OF AORTA

Instruction by the examiner:

- Examine the pulse or examine the pulse and relevant or examine the CVS.

Presentation of a Case:

- Pulse: 70/min, normal in rhythm, high volume in upper limb, femoral pulse is very feeble. There is radio-femoral delay.
- BP: 220/110 mmHg in upper limb (and low in lower limb).
- JVP: Normal.
- Carotid pulse: High volume and vigorous.
- There is visible suprasternal, right carotid and supraclavicular pulsation.

On inspection:

- Visible cardiac impulse.
- Visible dilated tortuous artery around the scapula, anterior axilla and over the left sternal border (collateral vessels are best seen by sitting and bending forward, with arm hanging by the side).

On palpation:

- Apex beat: In left . . . intercostal space, heaving in nature.
- Thrill may be present over the collateral vessels.

On auscultation:

- Heart sounds are normal.
- Systolic murmur is present in . . . intercostal space, close to the sternum, better heard in fourth intercostal space posteriorly (site of coarctation).
- May be ejection click, ESM in aortic area and EDM (due to bicuspid aortic valve or dilatation of aortic valve due to aneurysm causing AR).
- Lung fields are clear.

My diagnosis is **Coarctation of aorta (CoA)**.

Q: Why is it a case of coarctation of aorta?

A: Because radial pulse is high volume, femoral pulse is feeble and there is radio-femoral delay. Also, BP is very high in upper limbs and very low in lower limbs.

Q: Why murmur in coarctation of aorta?

A: Due to increased flow through collateral vessels. Also, due to associated congenital bicuspid aortic valve.

READ THE FOLLOWING TOPICS IN RELATION TO COARCTATION OF AORTA

Q: What are the types of coarctation of aorta?

A: 2 types:

- Postductal (adult type): Commonly below the origin of left subclavian artery, where ductus arteriosus joins the aorta.
- Preductal (infantile type, 2%): Above the origin of left subclavian artery. In such case, left radial pulse is weak and rib notching on right side. May be associated with PDA. Without other communication, the patient does not survive.

Q: What are the sites of collaterals?

A: Due to severe narrowing of the aorta, there are formation of collateral circulation involving the periscapular, internal mammary and intercostal arteries. Can cause bruit.

Q: What type of hypertension develops and why?

A: Usually systolic hypertension, diastolic may be normal. Causes of hypertension are:

- Mechanical.
- Renin–angiotensin mechanism (due to coarctation, less blood flow to kidney).
- Resetting of baroreceptors.

Q: What is reverse coarctation?

A: When pulse is absent in upper limbs, but present in lower limbs, it is called reverse coarctation. It occurs in Takayasu's disease.

Q: What are the complications of coarctation of aorta?

A: As follows:

- Hypertension and its complication (LVF and CVA).
- Infective endocarditis.
- Rupture at the coarctation site.
- Dissecting aneurysm.
- Aneurysm of aorta.
- Subarachnoid haemorrhage (due to rupture of berry aneurysm of circle of Willis).

Q: What are the causes of death in coarctation of aorta?

A: As follows:

- Acute LVF.
- Cerebral haemorrhage.
- Dissecting aneurysm.
- Subarachnoid haemorrhage (due to rupture of aneurysm of circle of Willis).

Q: What are the associations in coarctation of aorta?

A: As follows:

- Bicuspid aortic valve (in 50% cases).
- VSD.
- PDA.
- Aneurysm of circle of Willis (5 to 10% cases).
- In female, Turner's syndrome.
- Occasionally, Marfan's syndrome.

N.B. Remember the following points:

- Coarctation of aorta is twice more in male than female. M:F ratio is 2:1.
- It is 7% of all congenital heart diseases.
- Even if hypertension, renal involvement is unusual and fundal changes are also unusual.

Q: What are the causes of coarctation?

A: As follows:

- Congenital (commonest).
- Rarely, may be acquired in trauma, Takayasu's disease.

Q: What are the **presentations** of coarctation of aorta?

A: As follows:

- May be asymptomatic.
- Headache, nose bleeding, claudication of lower limbs, cold legs (due to poor blood flow in lower limb).

Q: What **investigations** do you suggest?

A: As follows:

1. X-ray chest PA view. It shows:
 - Poorly developed aortic knuckle (or elongated aortic knuckle), cardiomegaly, post-stenotic dilatation of aorta.
 - Rib notching, mostly at the middle part posteriorly, due to enlargement of intercostal arteries from third rib downwards (first and second ribs are not affected, because intercostal arteries here arise from subclavian artery above the constriction).
 - Figure of **3** (constriction at coarctation, pre-stenotic and post-stenotic dilatation).
2. ECG (shows LVH).
3. Echocardiogram.
4. CT scan and CMR angiography are ideal for confirming the diagnosis. Aortography may also be done.

Q: What are the **causes** of **unilateral rib notching**?

A: As follows:

- Coarctation of aorta (before the origin of left subclavian artery).
- Blalock–Taussig shunt (iatrogenic, done in Fallot's tetralogy).
- Subclavian artery obstruction.
- Neurofibromatosis.
- Congenital.

Q: What are the **causes** of **bilateral rib notching**?

A: As follows:

- Coarctation of aorta (after the origin of left subclavian artery).
- Neurofibromatosis.
- Congenital.

Q: How to **treat** coarctation of aorta?

A: As follows:

1. Should be treated surgically as early as possible, preferably before 5 years of age. Surgical resection and end to end anastomosis is usually done.
2. If coarctation is extensive, then prosthetic vascular graft may be done.
3. If surgery is done during adolescence or adulthood, hypertension may persist in 70% cases, due to irreversible changes in arterioles or renal damage. If done in early childhood, hypertension usually resolves completely.
4. In older children and adults, balloon dilatation and stenting is an option, but many still prefer surgery.
5. Balloon angioplasty may be helpful, particularly after re-stenosis.

Prognosis after surgery:

- Surgical correction in childhood—25 year survival in 83%.
- If surgery is delayed until adulthood—25 year survival in 75%.
- Without surgery—25% live up to 50 years of age, cardiac failure occurs in 2/3rd over 40 years of age.
- In few cases, re-stenosis may occur, can be treated by balloon angioplasty.
- If operation is delayed, the patient may have persistent hypertension, because of irreversible changes in the arterioles.
- May develop paradoxical hypertension due to baroreceptor-induced increased sympathetic activity.
- Co-existent bicuspid aortic valve occurs in 50% cases, may lead to AS or regurgitation.

MARFAN'S SYNDROME

Instruction by the examiner:

- Look at the patient and do the relevants. Or, perform the general examination.
- Examine the heart and relevants.

Proceed as follows:

- Look at the patient (tall, lean and thin).
- Measure height from pubis to vertex and pubis to sole of foot. Lower segment > upper segment. Pubis:sole > pubis: vertex. Also, see height and arm span—arm span > height.
- Look at the palate, eyes, bony deformity and hyperextensibility of joints.
- Finally examine the heart.

Presentation of a Case:

- The patient is tall, lean and thin. Face is long and narrow. Both upper and lower limbs are disproportionately longer than the trunk.
- There is arachnodactyly (long, thin, spider fingers and toes). Hyperextensibility of joints.
- Lower segment > upper segment (mention the exact measurement in centimetre or inch).
- Arm span > height (mention the exact measurement in centimetre or inch).
- Eye shows—blue sclera, subluxation of lens, ectopia lentis usually upward and outward, iridodonesis, atrophy of iris.
- Palate is high arched.
- In chest—pectus excavatum, carinatum and kyphoscoliosis.
- In foot—high arch or pes planus.
- Heart—signs of AR or MR.

My diagnosis is **Marfan's syndrome**.



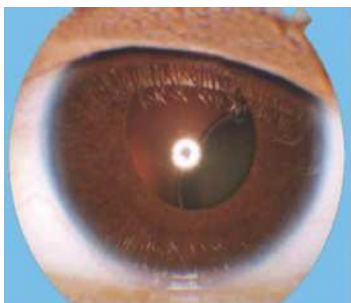
Arachnodactyly (hand)



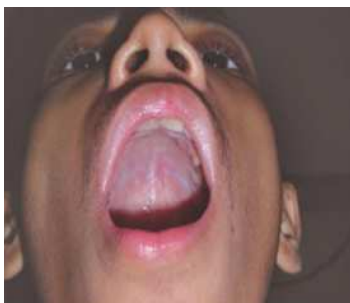
Arachnodactyly (fingers and toes)



Steinberg sign



Dislocation of lens



High arch palate



Pectus excavatum

Q: What is **Steinberg sign**?

A: When the thumb is adducted over the palm or completely enclosed within the clenched hand, it extends beyond the ulnar border.

READ THE FOLLOWING TOPICS IN RELATION TO MARFAN'S SYNDROME

Q: What is **Marfan's syndrome**? What are the **features**?

A: It is a connective tissue disorder inherited as autosomal dominant due to mutation in the fibrillin-1 gene, a component of extracellular matrix. Fibrillin gene is located in the long arm of chromosome 15 (15q21). Male and female are equally affected. It is characterized by triad of eye, skeletal and cardiac abnormalities.

1. Eye:

- Blue sclera.
- Subluxation or dislocation of lens (ectopia lentis).
- Iridodonesis (tremor of iris).
- Heterochromia iris (various colour of iris).
- Myopia.
- Retinal detachment.
- Glaucoma.

2. Skeletal:

- Tall, lean and thin, arachnodactyly, hyperextensibility of joints.
- High arched palate.
- Kyphosis or scoliosis. High pedal arch or pes planus.
- Pectus excavatum or carinatum or asymmetry of chest.

3. CVS:

- AR (due to aortic root dilatation, secondary to cystic medial necrosis of aorta).
- MR (due to mitral valve prolapse).

N.B. Marfan's syndrome may cause dissecting aneurysm, infective endocarditis. It may be associated with coarctation of aorta.

Diagnosis of Marfan's syndrome is made if:

- Positive family history and features of two different systems.
- Features in three different systems.

Q: What are the **associations** in Marfan's syndrome?

A: As follows:

- Cystic disease in lung, can cause spontaneous pneumothorax (may be recurrent), bullae, apical fibrosis, aspergilloma and bronchiectasis.
- Inguinal or femoral hernia.
- Small nodule or papule in skin of neck (Miescher's elastoma).

Q: What is your differential diagnosis and how to differentiate?**A:** Homocystinuria (due to deficiency of enzyme cystathionine synthetase).

Features	Homocystinuria	Marfan's Syndrome
1. Inheritance	AR.	AD.
2. Lens	Dislocated downward.	Dislocated upward.
3. Skeletal abnormality	Osteoporosis—common.	Osteoporosis—less common, but flat foot, scoliosis, pectus excavatum are common.
4. Aortic regurgitation	Rare.	Common.
5. Mental retardation	Common.	No.
6. Vascular complication	Prone to develop thrombosis.	No.
7. Life expectancy	Reduced from cardiovascular risk.	May be normal.
8. Test (urine)	Cyanide nitroprusside (positive).	Cyanide nitroprusside (negative).
9. Spectroscopic examination (urine)	Homocystine detected.	No.
10. Pyridoxine	May respond.	No.

Q: What are the complications or causes of death in Marfan's syndrome?**A:** As follows:

- Dissecting aneurysm.
- Heart failure.
- Infective endocarditis.

Q: What investigation should be done in Marfan's syndrome?**A:** As follows:

- X-ray chest (may be normal, may show features of aortic aneurysm, unfolding or wide mediastinum. Pneumothorax or scoliosis may be present).
- ECG (to see any arrhythmia).
- Echocardiogram (shows mitral valve prolapse, aortic regurgitation, MR, aortic root dilatation).
- CT or CMR (to see aortic dilatation).

Q: How to treat Marfan's syndrome?**A:** As follows:**1. Medical treatment:**

- β -blocker: It reduces aortic dilatation and prevents the risk of aortic rupture or dissecting aneurysm. Atenolol is more preferable.
- ACE receptor blocker: In Marfan's syndrome, there is upregulation of TNF- β , which is specifically inhibited by ACE blocker. It prevents aortic root dilatation.
- Prophylaxis for infective endocarditis.

2. Surgical treatment:

- Elective replacement of ascending aorta and aortic valve in patient with progressive dilatation of aorta (>5 cm).

3. Advice to the patient:

- Should avoid strenuous exercise to prevent aortic dissection.
- Genetic counselling and orthopaedic measures.
- Regular checkup, echocardiography should be done annually.

Q: What is the effect of pregnancy in Marfan's syndrome?

A: Pregnancy is well tolerated, if no serious cardiac problem. It is avoided, if aortic root dilatation is >4 cm with AR. Maternal death may occur due to aortic dissection during pregnancy. Early premature abortion may also occur. Echocardiogram should be done every 6 to 8 weeks throughout pregnancy and 6 months post-partum. BP should be regularly monitored.

Vaginal delivery is possible. Caesarean section is not done routinely. If aortic root is >4.5 cm, delivery should be done at 39 weeks by induction or Caesarean section. β -blocker should be continued throughout pregnancy.

DEXTROCARDIA

Instruction by the examiner:

- Examine the precordium.

Presentation of the Case:

- Apex beat is absent on left side, but present on right side, in . . . intercostal space, . . . cm from midline.
- Heart sounds are less heard in left side, but better heard in right side of chest.

My diagnosis is **dextrocardia**.

Q: What is **dextrocardia**?

A: When heart is on the right side of chest, but other viscera remain on their usual sites, it is called dextrocardia.

Q: What is **situs inversus**?

A: Dextrocardia with reversal of sites of other viscera (stomach on right side, liver on left side, right lung is on the left side, left lung is on the right side and the appendix on the left side, spleen on the right side).

Q: What is **levocardia**?

A: When heart is on left side, but there is reversal of the site of other viscera, it is called levocardia (stomach on right side, liver on the left side, right lung is on the left side and left lung is on the right side).

Q: What is **mesocardia**?

A: When cardiac apex is in the midline, it is called mesocardia.

Q: If the patient has dextrocardia, what **else** do you want to see?

A: Lung base for crepitations and clubbing (bronchiectasis) and associated with Kartagener syndrome. Also need to see liver for situs inversus.

Q: Suppose a patient has dextrocardia. Suggest **one investigation**.

A: PNS X-ray (to see frontal sinusitis or agenesis in Kartagener syndrome).

Q: What is **Kartagener syndrome**?

A: It is characterized by:

- Dextrocardia.
- Bronchiectasis.
- Frontal sinusitis or frontal sinus agenesis.
- Other features include situs inversus, infertility, otitis media and ciliary immotility.

Q: What is the **prognosis** in situs inversus?

A: Usually normal lifespan.

Q: What is the **clinical importance** in situs inversus?

A: As follows:

- Diagnosis of appendicitis may be missed (it is on the left side).
- Liver disease may be missed and liver biopsy may be mistakenly done on right side.

N.B. Dextrocardia may occur in Turner's syndrome.

EXAMINATION OF PULSE

Instruction by the examiner:

- Examine the pulse, or examine the pulse and relevants or examine the pulse and auscultate the heart.

If it is asked to examine the pulse, **any of the following findings** may be present:

- Irregular pulse (due to atrial fibrillation and multiple ectopics).
- High volume pulse or water hammer pulse.
- Bradycardia (due to complete heart block).
- Unequal radial pulse.
- Absent pulse (due to Takayasu's syndrome).
- Radio-femoral delay and radio-radial delay or inequality.

(See radial pulse. Look for rate, rhythm, volume, character, pulse delay and condition of the vessel wall. Finally, examine all other pulses and compare on both sides).

Q: What are the **causes** of irregular pulse?

A: See page 132.

Q: Is **collapsing** and **high volume** pulse synonymous?

A: No. Collapsing pulse is a high volume pulse, but all high volume pulses may not be collapsing.

Q: If **collapsing** pulse is present, what **else** do you want to see?

A: It is usually common in AR. So, I want to check the B.P. and signs of AR:

- BP: High systolic, low diastolic and wide pulse pressure.
- Neck: Dancing carotid pulse.
- Heart: EDM.

Q: What are the **causes** of bradycardia?

A: See page 132.

Q: What are the **causes** of unequal radial pulse? What are the **causes** of absent radial pulse?

A: As follows:

Causes of Unequal Radial Pulse:

- Atherosclerosis (usually elderly).
- Congenital anomaly or aberrant radial artery. Coarctation of aorta (before the origin of left subclavian artery).
- Dissecting aneurysm.
- Takayasu's disease.
- Occlusion of subclavian artery (by ribs and neoplasm).
- Aneurysm of aortic arch.
- Iatrogenic (Blalock–Taussig shunt in TOF).

Causes of Absent Radial Pulse:

- Anatomical aberration.
- Blockage by embolism or narrowing.
- Takayasu's syndrome.
- Iatrogenic (Blalock–Taussig shunt in TOF and AV fistula for haemodialysis).
- Dissecting aneurysm.
- Coarctation of aorta (before the origin of left subclavian artery).
- Brachial artery catheter with poor technique or tied during surgery.

N.B. Remember, scar mark with thrill in wrist indicates AV fistula for haemodialysis.

ATRIAL FIBRILLATION (IRREGULAR PULSE)

Instruction by the examiner:

- Examine the pulse. Or, Examine the pulse and relevants.
- Examine the pulse and auscultate the heart.

Presentation of Irregular Pulse:

- Pulse is 110/min, irregularly irregular (irregular in rhythm and volume).

My diagnosis is **Irregularly irregular pulse**.

Q: What do you think the **causes** in this case?

A: As follows:

- Atrial fibrillation.
- Multiple ectopics.

Q: How to **differentiate** between AF and multiple ectopics in bedside?

A: By physical exercise—ectopics will disappear or diminish, but atrial fibrillation will be more prominent or worse (ECG for confirmation, see below).

Q: What are the **ECG** findings in AF?

A: P is absent (P may be replaced by small fibrillatory ‘f’ wave) and RR interval is irregular.

Q: What are the **causes of irregularly irregular pulse**?

A: As follows:

- Atrial fibrillation.
- Multiple ectopics.
- Atrial flutter with variable block.
- Paroxysmal atrial tachycardia with variable block.

Q: What **relevants** do you want to examine in atrial fibrillation?

A: As follows:

- Heart (heart rate to see pulse deficit, mitral valvular or other cardiac disease).
- Thyroid status (warm sweaty hands, tremor of outstretched hands, tachycardia, exophthalmos and thyroid gland).
- History of IHD and hypertension.
- History of other diseases causing AF (see below).

READ THE FOLLOWING TOPICS IN RELATION TO ATRIAL FIBRILLATION

Q: What is **atrial fibrillation**?

A: Atrial fibrillation is an arrhythmia in which atria beats rapidly (300 to 600/min), chaotically and ineffectively, while ventricles respond at irregular intervals, producing the characteristic irregularly irregular pulse.

Q: What are the presentations?**A:** As follows:

1. Asymptomatic, may be detected during examination of the pulse.
2. Symptomatic:
 - Palpitation,
 - Breathlessness.
 - Weakness, dizziness, giddiness.
 - Features of primary disease.
 - Features of complications such as heart failure, embolism (commonly CVD with hemiplegia).

Q: What are the complications of AF?**A:** As follows:

- Systemic and pulmonary embolism (systemic from left atrium and pulmonary from right atrium). Annual risk is 5% (1 to 12).
- Heart failure.

Q: What are the causes of AF?**A:** As follows:

1. Commonest:
 - Chronic rheumatic heart disease, usually with MS.
 - Ischaemic heart disease (commonly, acute myocardial infarction).
 - Thyrotoxicosis.
 - Hypertensive heart disease.
 - Idiopathic or lone AF (10% cases).
2. Others :
 - Chronic constrictive pericarditis.
 - Acute infection (pneumonia).
 - Cardiomyopathy.
 - Thoracic surgery.
 - Cardiac surgery.
 - Acute pericarditis.
 - Electrolyte imbalance (hypokalaemia, hyponatraemia).
 - Congenital heart disease (ASD).
 - Alcohol abuse.
 - Sick sinus syndrome.
 - Pulmonary embolism.

N.B. Remember the following points:

- Commonest 5 causes should always be mentioned sequentially.
- Mention the causes according to the age of the patient in that particular case (see below).

Q: If the patient is **young**, what are the **causes** of atrial fibrillation?

A: As follows:

1. Chronic rheumatic heart disease with valvular lesions, commonly MS.
2. Thyrotoxicosis.
3. Others:
 - Atrial septal defect (ASD).
 - Acute pericarditis.
 - Myocarditis.
 - Pneumonia.

Q: If the patient is **elderly**, what are the **causes** of atrial fibrillation?

A: As follows:

- Coronary artery disease (commonly acute myocardial infarction).
- Thyrotoxicosis.
- Hypertension.
- Lone atrial fibrillation (idiopathic in 10% cases).
- Others: See above (unusual or less in chronic rheumatic heart disease).

Q: What are the **non-cardiac causes** of AF?

A: See above.

Q: What is **lone atrial fibrillation**?

A: Lone atrial fibrillation means atrial fibrillation without any cause. Genetic predisposition may be responsible.

- 50% patients with paroxysmal atrial fibrillation and 20% with persistent or permanent atrial fibrillation have no cause and heart is normal.
- Lone atrial fibrillation usually occurs below 60 years of age.
- It may be intermittent, later may become permanent.
- Prognosis: Low risk of CVD (0.5% per year). Usually life span is normal.

Q: If a patient with AF is **unconscious**, what is the likely cause?

A: CVD due to cerebral embolism (usually with right sided hemiplegia).

Q: What are the **types** of AF?

A: 2 types according to **heart rate** and 5 types according to clinical presentations:

1. According to heart rate, 2 types:
 - Fast AF (pulse >100/min).
 - Slow AF (pulse <100/min).
2. Clinical classification: 5 types-
 - First detected—not diagnosed previously, irrespective of duration or severity of symptoms.
 - Paroxysmal—self limiting, stops spontaneously within 48 hours, may be within 7 days in some cases. If cardioversion is done within 7 days, also called paroxysmal.
 - Persistent—continuous >7 days, including episodes that are terminated by cardioversion or by drugs after 7 days or more.
 - Longstanding persistent—continuous >1 year, when it is decided for rhythm control intervention.
 - Permanent—continuous, with a joint decision between the patient and physician, so rhythm control interventions are not pursued or attempted to regain sinus rhythm.

Q: How to investigate AF?**A:** As follows:

- ECG.
- Chest X-ray.
- Serum electrolytes, urea, creatinine.
- CBC.
- Echocardiogram.
- Thyroid function studies.
- Other investigations: according to the cause.

Q: How to treat AF?**A:** Aim of treatment:

- Control of heart rate.
- Restoration of sinus rhythm and prevention of recurrence.
- Treatment of primary cause.

Details of history, physical examination and investigation should be done to find out the cause.

Acute management:

1. When AF is due to an acute illnesses, such as alcohol toxicity, chest infection or hyperthyroidism, this should be treated, which restores sinus rhythm.
2. In other cases, following treatment should be given:

To control rate—digoxin, β -blocker or calcium channel blocker (verapamil or diltiazem) may be given.

If no response, cardioversion (medical or DC shock) should be done as follows-

- Intravenous infusion of antiarrhythmic drug such as flecainide, propafenone, vernakalant or amiodarone. Oral flecainide or propafenone may be given.
- If no response—DC shock should be given.

Long term treatment (according to the types):**1. Paroxysmal atrial fibrillation:**

- If asymptomatic: no treatment is necessary. Treatment of primary cause should be done and regular follow up the case should be done.
- If symptoms are present: β -blocker is usually given. If no response, other drugs such as flecainide or propafenone may be given.
- Amiodarone is effective in prevention.
- Low dose aspirin to prevent thromboembolism.
- If bradycardia (in sinoatrial disease): Permanent over drive atrial pacing (60% effective).
- In intractable cases: Radiofrequency ablation may be required, if no structural heart disease (70% effective).

2. Persistent atrial fibrillation:

- To control heart rate: β -blocker, digoxin or calcium channel blocker (verapamil, diltiazem). Combination of digoxin and atenolol may be used.
- To control rhythm: DC cardioversion. May be repeated, if relapse occurs.
- β -blocker or amiodarone may be used to prevent recurrence.
- If no response: Transvenous radiofrequency ablation may be done (It induces complete heart block. So, permanent pacemaker should be given. This is known as 'patch and ablate strategy').

N.B.: Patient should be anticoagulated with warfarin (INR 2.0 to 3.0) or dabigatran 150 mg twice daily for 3 weeks before cardioversion (unless atrial fibrillation is of <48 hours duration) and at least 4 weeks after the procedure.

Q: What are the **new oral anticoagulants (NOAC)** for the treatment of AF?

A: As follows:

- Thrombin inhibitor—Dabigatran.
- Factor Xa inhibitor—Rivaroxaban, Edoxaban, Apixaban.

Q: What are the **advantages and disadvantages of NOAC?**

A: As follows:

- Advantage—NOACs have a rapid onset of action, shorter half-life, few food and drug interactions. Do not require INR testing, equally effective as and safer than warfarin.
- Disadvantage—These agents require dose reduction or avoidance in patients with renal impairment, in elderly or those with low body weight.

Q: What is the **role of anticoagulant in atrial fibrillation?**

A: Anticoagulation is indicated in AF related to rheumatic mitral stenosis or in mechanical prosthetic heart valve. In patients with non-valvular AF (in the absence of mitral stenosis, artificial heart valves or mitral valve repair), a scoring system known as CHA₂DS₂VASc is used to determine the need for anticoagulation.

CHA₂DS₂VASc Risk Score for assessing risk of stroke and for selecting antithrombotic therapy for patients with atrial fibrillation:

Risk Factors		Score/Points
C	Congestive heart failure	1
H	Hypertension	1
A2	Age ≥ 75	2
D	Diabetes mellitus	1
S2	Stroke/TIA/thromboembolism	2
V	Vascular disease (aorta, coronary or peripheral arteries)	1
A	Age 65 to 74	1
Sc	Sex category: female	1
Annual risk of stroke		
0 points = 0% risk: No prophylaxis.		
1 point = 1.3% risk: Anticoagulant (oral) or aspirin.		
2+ points = 2.2% risk: Oral anticoagulant.		

N.B. Remember the following points:

- In lone atrial fibrillation: Aspirin may be given to prevent thromboembolism.
- Age <65 years and young with no structural heart disease: Aspirin may be beneficial. No warfarin.
- Target INR following anticoagulation is 2 to 3.

SLOW PULSE RATE (COMPLETE HEART BLOCK)

Instruction by the examiner:

- Examine the pulse or examine the CVS.
- Examine the pulse and precordium.

Presentation of a Case:

- Pulse: 40/min, high volume, normal rhythm, no radio-femoral delay, condition of the vessel wall is normal.
- B.P.: 150/70 mmHg (wide pulse pressure).
- Neck vein: Occasional cannon 'a' waves are present.
- In the precordium: Variable intensity of first heart sound. There is a systolic flow murmur (due to increased stroke volume).

My diagnosis is **Bradycardia**.

Q: What is the most likely cause in this case?

A: As follows:

- Complete heart block
- Drugs such as β -blocker, digoxin, verapamil.

Q: What are the causes of bradycardia?

A: As follows:

- Sinus bradycardia due to any cause.
- Second degree heart block.
- Complete heart block.
- Nodal rhythm.

Causes of sinus bradycardia:

1. Physiological (due to increased vagal tone): Athlete, during sleep.
2. Pathological:
 - Acute inferior myocardial infarction.
 - Myxoedema (due to reduction of sympathetic activity).
 - Hypothermia. Raised intracranial tension (due to inhibitory effect on sympathetic outflow). Obstructive jaundice (due to deposition of bilirubin in conducting system).
 - Drugs (digoxin, β -blockers, amiodarone and verapamil).

Q: Why variable intensity of first heart sound and systolic murmur in CHB?

A: As follows:

- Variable intensity of first heart sound is due to loss of AV synchrony.
- Systolic flow murmur is due to increased stroke volume.

Q: What is the mechanism of cannon wave?

A: Due to loss of AV synchrony, when atria contracts against closed tricuspid valve, backward pressure produces cannon wave.

Q: What is the **ECG change** in CHB?

A: Complete dissociation between P and QRS heart rate is <40 beats/minute.

Q: If **pulse rate is high**, what are the likely **causes** of CHB?

A: As follows:

- Pulse rate is high in congenital complete heart block and does not require treatment.
- If the block occurs more proximally in AV node (narrow complex escape rhythm).

Q: What are the **presentations** of complete heart block?

A: As follows:

- Dizziness or giddiness, weakness.
- Blackout or sudden loss of consciousness.
- Syncope (Stokes Adams attack).

READ THE FOLLOWING TOPICS IN RELATION TO CHB

Q: What are the **causes** of complete heart block?

A: Commonest causes are:

1. **Acute CHB:** Acute myocardial infarction (commonly inferior).
2. **Chronic CHB: Idiopathic fibrosis due to-**
 - Progressive fibrosis of distal His–Purkinje system (Lev’s disease), in elderly.
 - Progressive fibrosis of proximal His–Purkinje system (Lenegre’s disease), in younger.

Other **causes** of CHB (usually chronic):

- Cardiomyopathy (ischaemic or idiopathic dilated), myocarditis.
- Calcific aortic stenosis.
- Drugs (digoxin, β -blockers, amiodarone, verapamil, diltiazem).
- Cardiac surgery (aortic valve replacement, VSD repair and CABG).
- Radiofrequency ablation of AV node and pacemaker implantation.
- Infiltrative disease (sarcoidosis, amyloidosis and haemochromatosis).
- Infection (infective endocarditis, Chagas’ disease and Lyme disease).
- Collagen disease (SLE, rheumatoid arthritis).
- Congenital complete heart block: common in child of SLE mother, transposition of great vessels.
- Neuromuscular (Duchenne muscular dystrophy).

Q: What is the **cause** of congenital heart block?

A: Congenital heart block usually occurs, if the mother is suffering from SLE due to the presence of anti-Ro (SSA) antibody, which crosses the placenta and causes congenital heart block.

Q: What are the **signs** of complete heart block?

A: As follows:

- Pulse: Bradycardia, 20 to 40 beats/min, high volume, does not increase by exercise or injection atropine.
- BP: High systolic, normal diastolic and wide pulse pressure.
- Neck vein: Cannon waves (large ‘a’ wave) may be present.
- Heart sounds: Variable intensity of first heart sound.
- Murmur: Systolic flow murmur (due to increased stroke volume).

N.B.: When AV conduction fails completely, atria and ventricle beat independently (AV dissociation). Ventricular activity is maintained by an escape rhythm from 2 sites-

- *Arising in AV node or bundle of His (narrow QRS complexes) with more heart rate.*
- *Distal Purkinje tissues (broad QRS complexes) with slow heart rate. Stokes Adams attack usually occurs.*

Q: How to **treat** complete heart block?

A: If symptomatic, permanent pacemaker should be given. Implantable cardioverter defibrillator (ICD) indicated in those with severe left ventricular dysfunction (>0.30 s duration).

Q: What is **Stokes–Adams attack**? What are the **clinical features** and **treatment**?

A: It is the brief attack of syncope or blackout in a patient with complete heart block due to ventricular asystole. Stokes–Adams attack may also occur in Mobitz type II heart block, ventricular tachycardia or fibrillation, sinoatrial disease. Clinical features are:

- Syncope or blackout with or without preceding dizziness.
- During attack patient is unconscious, looks pale and may have convulsion.
- If asystole persists, there may be cyanosis, pulse is absent, incontinence of urine, pupil is fixed and dilated, plantar is extensor.
- Usually consciousness recovers rapidly followed by flushing.

Treatment:

- Permanent pacemaker (even after a single syncopal attack).
- During attack: CPR should be done.

ABSENT PULSE (TAKAYASU'S DISEASE)

Instruction by the examiner:

- Examine the pulse or examine the pulse and precordium.

Presentation of a Case:

- All the pulses of upper limbs are absent, but present in lower limbs.
- Blood pressure is undetectable in the upper limb and normal or high in lower limb (to see BP in lower limb, a 18 cm cuff is required).
- Bruit is present (mention the location e.g., carotid).
- No other abnormality in CVS (occasionally evidence of AR are found).
- There may be less development of upper part of the body.

My diagnosis is **Absent pulse**, which may be due to **Takayasu's disease** (pulseless disease or aortic arch syndrome).

Q: What are the **causes** of absent radial pulse?

A: As follows:

- Anatomical aberration.
- Blockage by embolism or narrowing.
- Takayasu's syndrome.
- Iatrogenic (Blalock–Taussig shunt in TOF and AV fistula for haemodialysis).
- Dissecting aneurysm.
- Coarctation of aorta (before the origin of left subclavian artery).
- Brachial artery catheter with poor technique or tied during surgery.

READ THE FOLLOWING TOPICS IN RELATION TO TAKAYASU'S DISEASE

Q: What is **Takayasu's disease**?

A: It is a chronic, inflammatory, granulomatous panarteritis of unknown cause involving the elastic arteries, commonly aorta and its major branches, carotid, ulnar, brachial, radial and axillary. Occasionally, may involve pulmonary artery, rarely abdominal aorta, renal artery resulting in obstruction.

Common in female, F:M ratio is 8:1.

Q: What are the **pathological changes** in Takayasu diseases?

A: Panarteritis, intimal hyperplasia, thickening of media and adventitia, later on fibrosis.

Q: What are the **clinical features**? What are the **types**?

A: Common in young female, 25 to 30 years, more in Asians.

- In acute stage—fever, malaise, weight loss, arthralgia, myalgia and high ESR, CRP.
- In chronic case—dizziness, giddiness, headache, syncope, claudication in the upper limb.
- There may be AR, renal artery stenosis or anginal pain.
- Hypertension in 32 to 93%.

Types of Takayasu's disease—4 types:

- Type 1: Involves aortic arch and its major branches.
- Type 2: Involves descending aorta and abdominal aorta.
- Type 3: Involves both type 1 and type 2. This may be complicated by aortic regurgitation.
- Type 4: Involves the pulmonary arteries.

Q: How to diagnose Takayasu's arteritis?

A: Takayasu arteritis is diagnosed by presence of 3 or more of the following criteria:

- Age of onset ≤ 40 years.
- Claudication of the extremities.
- Decreased pulsation of one or both brachial arteries.
- BP difference > 10 mmHg between left and right arm.
- Bruit over one or both subclavian arteries or the abdominal aorta.
- Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the upper or lower extremities that is not due to arteriosclerosis, fibromuscular dysplasia or other causes.

Q: What investigations should be done?

A: As follows:

- CBC (shows high ESR and normocytic normochromic anaemia).
- CRP—high.
- Chest X-ray shows cardiomegaly and widening of aorta.
- Serum immunoglobulin is high.
- MRI—helpful to detect inflammatory thickening of the affected vessel walls.
- CT angiography—helpful to detect stenosis, occlusion and condition of arteries.
- Aortography of aortic arch and its branches, renal angiogram shows narrowing, coarctation and aneurysmal dilatation.

Q: How to treat Takayasu's disease?

A: As follows:

1. High dose steroid: Prednisolone 40 to 60 mg daily or 1 to 2 mg/kg.
2. If refractory to steroid or difficult to taper steroid—methotrexate up to 25 mg weekly.
3. Cyclophosphamide may be used in resistant case.
4. If difficult to taper steroid, or in refractory case—methotrexate 25 mg per week may be given with prednisolone.
5. Or, methotrexate, mycophenolate mofetil or azathioprine may be added with prednisolone, which is more effective than prednisolone alone.
6. Anti-TNF agents such as etanercept, infliximab may be given in relapse.
7. Reconstructive vascular surgery in selected case. Angioplasty, stenting or bypass surgery may be done, if there is vascular complication.
8. Treatment of hypertension.

Q: What are the **complications** of Takayasu's disease? What is the **prognosis**?

A: As follows:

- Ischaemia.
- Heart failure.
- Stroke (Intracranial haemorrhage).
- Seizures.
- Organ failure.
- Retinopathy.
- Renovascular hypertension.

Prognosis: With appropriate treatment, the 5-year survival is 83%.

PERICARDIAL EFFUSION

Instruction by the examiner:

- Examine the CVS.

Presentation of a Case:

- Pulse: 110/min (tachycardia), low volume, may be pulsus paradoxus (indicates cardiac tamponade).
- JVP: Raised, Kussmaul's sign positive (raised JVP during inspiration).
- BP: Low systolic, normal diastolic and narrow pulse pressure.

On inspection:

- Nothing significant.

On palpation:

- Apex beat: could not be palpated.

On percussion:

- Area of cardiac dullness is increased.

On auscultation:

- Heart sounds are muffled (or distant).
- Bronchial sound at the left inferior angle of scapula (Ewart's sign, which is due to the compression of the base of the left lung due to enlarged heart).

My diagnosis is **Pericardial effusion**.

Q: How to confirm your diagnosis?

A: 2-D echocardiogram (it shows **echo free** zone). Pericardiocentesis is definitive for diagnosis.

Q: If echocardiogram is not available, how to diagnose pericardial effusion?

A: Chest X-ray in a Trendelenburg position (base of heart will be wide).

Q: What are the ECG findings in pericardial effusion?

A: Low voltage tracing and sinus tachycardia.

READ THE FOLLOWING TOPICS IN RELATION TO PERICARDIAL EFFUSION

Q: What are the causes of pericardial effusion?

A: As follows:

- Following acute infective pericarditis (bacterial and viral).
- Tuberculosis.
- Collagen diseases (SLE, rheumatoid arthritis).
- Cardiac causes (post MI, postcardiotomy, Dressler's syndrome).
- Myxoedema.
- Lymphoma.
- Neoplasm (secondary from carcinoma of breast and bronchial carcinoma).
- Dialysis during CKD or AKI.
- Dissecting Aortic aneurysm.
- Others—trauma, after radiotherapy.

Q: What are the signs of pericardial effusion?**A:** As follows:

1. Pulse—low volume, tachycardia, there may be pulsus paradoxus (indicates cardiac tamponade).
2. JVP—raised, Kussmaul's sign is positive (rise of JVP during inspiration. Normally, JVP falls during inspiration). Raised JVP with sharp rise and 'y' descent (Friedreich's sign).
3. Blood pressure—low systolic, normal diastolic and narrow pulse pressure.
4. In the precordium-
 - Apex beat is difficult to palpate. If palpable, it is within the area of cardiac dullness.
 - Area of cardiac dullness is increased (on percussion).
 - Heart sounds are muffled or distant.
 - Bronchial sound at the left inferior angle of scapula (Ewart's sign).
5. Liver is enlarged and tender.

Q: What investigations are done in pericardial effusion?**A:** As follows:

1. Chest X-ray PA view (shows heart is enlarged in TD, globular, pear shaped with clear margin and lung fields are oligoemic).
2. Full blood count (ESR high in TB and SLE).
3. ECG (low voltage tracing and tachycardia).
4. Echocardiogram—shows echo free zone. Colour Doppler shows increased flow through tricuspid and pulmonary valve, decreased flow through mitral valve during inspiration.
5. Pericardiocentesis:
 - To see the physical character (whether straw, haemorrhagic, turbid etc.).
 - Analysis of pericardial fluid to find out the cause (Gram staining, cytology, biochemistry, culture and sensitivity, AFB, ADA, malignant cell).
 - Pericardial biopsy may be done.
6. Cardiac CT or MRI (helpful to see haemopericardium or loculated pericardial effusion).
7. Other investigations according to suspicion of causes:
 - TB (MT, sputum for AFB).
 - Collagen disease (RA test, ANA, anti-ds DNA).
 - Hypothyroidism (FT₃, FT₄ and TSH).
 - If palpable lymph node, biopsy should be done.

Q: What are the findings in tuberculous pericardial effusion?**A:** Pericardial fluid shows:

- Straw coloured.
- Cytology shows high lymphocyte.
- Biochemistry shows high protein and low sugar.
- ADA is high.

Isolation of organism from pericardial fluid by:

- AFB staining (positive in 25% cases).
- Culture (Löwenstein–Jensen media).
- PCR.

Q: How to treat pericardial effusion?**A:** As follows:

- If tuberculosis—antituberculosis plus prednisolone.
- If bacterial cause—broad spectrum antibiotic.
- Other treatment of primary cause (e.g., hypothyroidism, SLE, RA, lymphoma).
- Pericardiocentesis—if cardiac tamponade develops.

Q: What are the causes of recurrent pericardial effusion? How to treat?**A:** Mostly due to malignancy, may be in CKD. In such case, following treatments are given:

- Pericardial fenestration (creation of window in the pericardium) is done to allow slow release of fluid in the surrounding tissue.
- Surgical drainage or partial pericardiectomy may also be necessary.

Q: How pericardiocentesis is done?**A:** Done under ultrasonographic or echocardiographic guidance. Aspiration needle is introduced through left costo-xiphoid junction, directed upward, backward and towards the left shoulder. Needle may also be introduced lateral to the apex beat.**Q: What are the complications of pericardiocentesis?****A:** Complications of pericardiocentesis:

- Injury to coronary artery and ventricles.
- Dysrhythmia.
- Bleeding (which may aggravate cardiac tamponade).

Q: What is cardiac tamponade?**A:** It is a state of compression of heart in rapidly developing pericardial effusion. It interferes with the diastolic filling of heart and the patient develops features of shock. If rapid accumulation of fluid, even 200 mL can cause cardiac tamponade. However, if slow accumulation of fluid occurs, 2000 mL may be required for cardiac tamponade.**Q: What are the causes of cardiac tamponade?****A:** As follows:

- Trauma or cardiac surgery (causing haemopericardium).
- Malignancy (repeated effusion may occur).
- Myocardial rupture.
- Dissecting aortic aneurysm.
- Sometimes, any cause of pericardial effusion can cause.

Q: What are the features of cardiac tamponade?**A:** As follows:

1. Symptoms:
 - Heaviness and compression in chest, usually retrosternal.
 - Palpitation.
 - Dyspnoea.
 - Features of shock.
2. Signs: See above in pericardial effusion.

Q: How to treat?**A:** As follows:

- It is a medical emergency. Pericardiocentesis should be done.
- Treatment of primary cause.

CHRONIC CONSTRICTIVE PERICARDITIS

Instruction by the examiner:

- Examine the CVS.

Presentation of a Case:

- Pulse: 120/min (tachycardia), low volume. Pulsus paradoxus may be present.
- JVP: Raised, rapid 'y' descent. Kussmaul's sign positive (raised JVP on inspiration).
- BP: 100/70 mmHg.
- Fall of Y descent (Friedrich's sign).

On inspection:

- Nothing significant.

On palpation:

- Apex beat: Palpable (in the left . . . intercostal space, . . . cm from the midline), normal.

On auscultation:

- 1st and 2nd heart sounds are normal. Pericardial knock (a 3rd heart sound, due to rapid ventricular filling).

My diagnosis is **Chronic constrictive pericarditis**.

Q: What **other signs or relevants** do you like to look for?

A: Ascites (early feature), oedema (late feature) and hepatomegaly.

Q: What is **chronic constrictive pericarditis**?

A: It is a disorder characterized by progressive thickening, fibrosis and calcification of pericardium. Commonly, involves right side of the heart.

Q: What are the **presentations and signs** of chronic constrictive pericarditis?

A: Most features are due to systemic venous congestion which are the hallmarks of chronic constrictive pericarditis. **Symptoms:**

- Weakness, dizziness, giddiness, anorexia, nausea and vomiting.
- Cough, breathlessness on exertion, may be orthopnoea, paroxysmal nocturnal dyspnoea.
- Abdominal swelling, later ankle swelling.

Signs:

- Tachycardia, low volume pulse.
- Pulsus paradoxus may be present.
- JVP: Raised, rapid y descent (Friedrich's sign). Kussmaul's sign positive (raised JVP on inspiration).
- Pericardial knock (a third heart sound due to rapid ventricular filling).
- Enlarged tender liver.
- Ascites.
- Peripheral oedema later on.

READ THE FOLLOWING TOPICS IN RELATION TO CONSTRICTIVE PERICARDITIS

Q: What are the **causes** of chronic constrictive pericarditis?

A: As follows:

- Infection (TB and Coxsackie B infection).
- Haemopericardium (due to trauma, myocardial rupture after infarction and dissecting aneurysm).
- Collagen disease (rheumatoid arthritis).
- Cardiac operation (open heart surgery).
- Mediastinal irradiation.
- Drug—dopamine agonis such as cabergoline and pergolide.
- Fungal infection (histoplasmosis).
- Rarely, after acute purulent pericarditis.
- Idiopathic.

N.B. Calcification commonly involves right side of the heart and can be seen by fluoroscopy. Calcification does not always mean constriction. Rheumatic fever does not cause chronic constrictive pericarditis.

Q: What are the **complications** of chronic constrictive pericarditis?

A: As follows:

- Atrial fibrillation (in 30% cases).
- Ascites.
- Myocardial fibrosis.

Q: What **investigations** are done?

A: As follows:

1. Chest X-ray (PA and lateral view): shows relatively small heart, pericardial calcification in 50% cases.
2. ECG (low voltage tracing, tachycardia, T inversion).
3. Echocardiogram (shows thick calcified pericardium, small ventricular cavities with normal wall thickness, large atrium, dilatation of inferior vena cava, abnormal septal motion and immobile heart).
4. Colour Doppler (shows reduction of flow along mitral valve and pulmonary vein during inspiration. Opposite occurs during expiration).
5. CT scan or CMR.
6. Cardiac catheterization shows that diastolic pressure is equal in left and right ventricles, end-diastolic pressure is equal in left and right atrium.
7. Other investigations (according to suspicion of cause).
8. Endomyocardial biopsy: May be necessary to differentiate from restrictive cardiomyopathy in difficult cases.

Q: How to **treat** chronic constrictive pericarditis?**A:** As follows:

- Surgery—Complete resection of pericardium (helpful in 50% cases).
- If TB—pericardiectomy with anti-TB drug. If there is no calcification, only anti-TB drug should be given. If the haemodynamic status of the patient deteriorates after 4 to 6 weeks, pericardiectomy should be done.
- Treatment of primary cause should be done.
- After surgery—persistent constriction and myocardial fibrosis may be present. AF may occur after recovery.

Q: What are the **differential diagnoses** of chronic constrictive pericarditis?**A:** As follows:

- Restrictive cardiomyopathy.
- CCF.

Q: How to **differentiate** chronic constrictive pericarditis from CCF?**A:** As follows:

Features	CCF	Chronic Constrictive Pericarditis
1. Breathlessness	Common, more on exertion.	Not common in rest, occurs on exertion.
2. Pulsus paradoxus	No.	May be present.
3. JVP	Raised, no Kussmaul's sign.	Raised, Kussmaul's sign positive, may be 'y' descent.
4. Cardiomegaly	Present.	Absent.
5. Oedema	Early feature than ascites.	Ascites early, oedema late feature.
6. On auscultation	Murmur may be present.	Pericardial knock is present.

Q: How to **differentiate** chronic constrictive pericarditis from restrictive cardiomyopathy?**A:** As follows:

Features	Chronic Constrictive Pericarditis	Restrictive Cardiomyopathy
1. Apex beat	Not felt.	Well felt.
2. Heart	Normal and pericardial knock is present.	May be enlarged, LVH and LVF may be present.
3. ECG	Low voltage tracing, tachycardia.	Bundle branch block, Q wave may be present.
4. Echocardiogram	Changes in pericardium.	Myocardium is thick.
5. Colour Doppler	Respiratory variation in A:V flow.	No change.
6. CT or CMR	Pericardium is thick with calcification.	Thick ventricle.

ACUTE PERICARDITIS

Instruction by the examiner:

- Examine the CVS. Or, auscultate the precordium.

Presentation of a Case:

- Pulse: 80/min, normal in volume and character.
- JVP: Not raised.
- BP: 120/75 mmHg.

On inspection:

- Nothing significant.

On palpation:

- Apex beat: Palpable (in the left . . . intercostal space, . . . cm from the midline), no thrill, no palpable P₂.

On auscultation:

- Heart sounds are normal.
- There is pericardial rub in left third and fourth intercostal space near the left lower parasternal border, persists after holding the breath.

My diagnosis is **Acute pericarditis**.

Q: What are the **presentations or clinical features** of acute pericarditis?

A: Clinical features are:

Symptoms:

- Chest pain usually central or retrosternal, sharp or stabbing in nature, may radiate to the shoulder and neck.
- Pain is aggravated by movement, lying down, deep breathing, exercise and swallowing, it is relieved by sitting or bending forward.
- Other symptoms: according to cause (e.g., in TB, low grade fever, evening rise of temperature, night sweating, weight loss).

Signs: Pericardial rub-

- It is a high pitched, harsh, scratching, grating, leathery sound, to and fro in quality, better heard over the left lower parasternal area with the patient leaning forward (it is called the bare area of heart, the part of heart that is not covered by lung).
- Usually heard in systole, may be in diastole, augmented by pressing the stethoscope,
- Present after holding the breath (to differentiate from pleural rub).

READ THE FOLLOWING TOPICS IN RELATION TO ACUTE PERICARDITIS

Q: What are the **causes** of acute pericarditis?

A: As follows:

1. Infection-
 - Viral (Coxsackie B, echovirus, mumps, herpes, HIV).
 - Bacterial (*Staph aureus*, *Streptococcus*, *Pneumococcus*, *H. influenzae*, *Chlamydia*).
 - Tuberculous pericarditis.
 - Fungal (histoplasmosis, coccidioidomycosis, candida).
2. After acute myocardial infarction (usually on second or third day) or Dressler's syndrome (later).
3. Autoimmune—Rheumatic fever, collagen disease (SLE, scleroderma, rheumatoid arthritis).
4. Renal failure (an indication of urgent dialysis).
5. Malignancy:
 - Primary tumour of heart (mesothelioma).
 - Metastasis from carcinoma of bronchus, breast, lymphoma, leukaemia, melanoma.
6. Myxoedema.
7. Drugs (doxorubicin, cyclophosphamide, procainamide, hydralazine).
8. Post-surgical pericarditis (Post-pericardiotomy syndrome).
9. Others: Post-radiation, post-traumatic, idiopathic.

Q: What are the **commonest causes** of acute pericarditis?

A: Viral infection (such as Coxsackie B, Echo virus) and acute myocardial infarction.

Q: What is the **incidence of pericarditis after myocardial infarction**?

A: Pericarditis occurs in 20% cases, in the first few days after myocardial infarction, commonly anterior and STEMI with high serum cardiac enzymes, less (5 to 6%) with thrombolysis. Pericarditis may occur as Dressler's syndrome, 2 to 10 weeks after infarction.

Q: What **investigation** should be done in acute pericarditis?

A: As follows:

- ECG: shows ST elevation with upward concavity (chair shaped or saddle shaped).
- CXR PA view.
- Echocardiography.
- CT and cardiac MRI may be done in some cases.
- Others: according to suspicion of cause.

Q: How to **differentiate** acute pericarditis from acute MI by ECG?

A: As follows:

- In MI—ST elevation with upward convexity.
- In pericarditis—ST elevation with upward concavity.

Q: How to treat acute pericarditis?**A:** As follows:

1. To relieve pain: NSAIDs (indomethacin or ibuprofen or aspirin).
2. In severe or recurrent case: steroid (prednisolone) should be given.
3. If no response to steroid: azathioprine or colchicine may be given.
4. If recurrence with no response to medical treatment: pericardiectomy may be done.
5. Treatment of primary cause, such as:
 - Antibiotic, if bacterial infection.
 - Anti-Koch's therapy, if TB is suspected.

N.B. Idiopathic relapsing pericarditis may be present in 20% cases of acute pericarditis. Treatment is as above. If pericarditis persists 6 to 12 months following acute attack, it is considered chronic.

Q: What is Dressler's syndrome?

A: Dressler's Syndrome or post myocardial infarction syndrome is a late complication of myocardial infarction that occurs usually after few weeks or even months (2 to 10 weeks) after acute MI. It is characterized by (5 'P's):

- Pain (chest pain).
- Pyrexia.
- Pleurisy.
- Pericarditis (or pericardial effusion).
- Pneumonitis (or pulmonary infiltrate).

Treatment:

- High dose aspirin (600 to 900 mg) every 4 to 6 hours or other NSAID.
- In severe or in recurrent case—corticosteroid may be given.
- Anticoagulant should be discontinued (unless strong evidence for high risk of thromboembolism).

RHEUMATIC FEVER

Instruction by the examiner:

- Examine the knee joints (or other joints) or examine the lower limbs. What are your findings? What would you like to see in the heart?

Presentation of a Case: (Supposing Both Knee and Ankle Joints)

- Both the **knee** and **ankle** joints are swollen, skin is red and shiny, local temperature is raised and the joints are very tender.
- There is restricted movement of the joints (because of pain).

My **differential diagnoses** are:

- Acute rheumatic fever (if deformity is present, it is **against** RF).
- Reactive arthritis or Reiter's syndrome.
- Juvenile idiopathic arthritis (JIA or JCA).
- Seronegative arthritis (ankylosing spondylitis and enteropathic arthritis).
- Haemophilic arthritis.
- Rheumatoid arthritis.
- Psoriatic arthritis (if any skin lesion, nail change).
- Septic arthritis.
- Acute leukaemia.
- Acute gouty arthritis.
- Trauma.

Q: What is the **likely diagnosis** in this child?

A: Acute rheumatic fever.

Q: What **relevants** do you like to examine in RF?

A: As follows:

- I would like to examine the heart to see evidence of carditis (pericarditis, myocarditis and endocarditis).
- Erythema marginatum (pinkish rash with slightly raised margin, mostly over the trunk and limbs).
- Subcutaneous nodules (found over bony prominences, joints and tendons. These are small and painless, are found over the extensor surface).
- Rheumatic chorea.

Q: What are the **presenting complaints** of a patient with RF?

A: RF usually occurs in children and young adults. **Features** are:

- Migrating (fleeting), non-deforming polyarthritis involving the large joints (knee, ankle and elbow) and wrists with fever, may be continuous, high grade is the presenting feature in 75% cases.
- Palpitation and chest pain (due to carditis in 50% cases).
- Skin rash (erythema marginatum), subcutaneous nodules.
- Involuntary movement (chorea in 10 to 30% cases).
- Malaise, weakness and fatigue.

Q: What investigations should be done in RF?**A:** As follows:

- CBC, ESR (high ESR and leucocytosis).
- CRP: high.
- ASO titre: may be high, in adult >200, in children >300.
- Throat swab for C/S (to find *Streptococcus haemolyticus*).
- Chest X-ray (may show cardiomegaly, pulmonary oedema may be present).
- ECG.
- Echocardiography (to see valve abnormality and cardiomegaly).
- RA factor (to exclude RA) and ANA (to exclude SLE), if needed.

READ THE FOLLOWING TOPICS IN RELATION TO RHEUMATIC FEVER**Q: What is RF? What is the mechanism or pathogenesis of RF?**

A: It is a multisystem disorder, occurs as a sequela to pharyngitis by *Streptococcus β-haemolyticus* group A. It is due to autoimmune reaction between the antigen (M protein) of *Streptococcus haemolyticus* and cardiac myosin and sarcolemmal membrane protein (laminin). As a result, antibody is produced against streptococcal enzyme, causing inflammation in the endocardium, myocardium and pericardium as well as joints and skin. There is formation of 'Aschoff nodule' in heart only.

Q: What is Aschoff nodule?

A: It is a granulomatous nodule composed of central fibrinoid necrosis and multinucleated giant cells, surrounded by macrophage and T-lymphocytes. It occurs throughout the heart. It is pathognomonic of RF.

Q: Which joints are commonly involved in ARF?

A: Commonly large joints, ankle, wrist, knee and elbow (usually does not involve small joints of the hands and feet, rarely involves hip joint).

Q: What are the diagnostic criteria of RF?

A: It is diagnosed by 'Modified Jones criteria'. Following an attack of *Streptococcus pharyngitis*, there is usually a latent period of 1 to 3 weeks.

1. Major criteria:

- Carditis.
- Shifting or migrating polyarthritis involving the big joints (knee, elbow, ankle, wrist).
- Rheumatic chorea.
- Erythema marginatum.
- Subcutaneous nodule.

2. Minor criteria:

- Fever.
- Arthralgia.
- Previous history of RF.
- High ESR or CRP.
- Leucocytosis.
- First or second degree AV block in ECG.

3. Evidence of recent streptococcal infection

- Positive throat culture for group A streptococcus.
- Clinical history of scarlet fever.
- Raised ASO titre or other streptococcal antibody titre (anti-DNAse or antihyaluronidase).

Diagnosis is made by two or more major criteria or one major and two or more minor criteria plus supportive evidence of streptococcal infection.

Q: What are the signs of carditis?

A: RF can cause carditis involving endocardium, myocardium and pericardium, called pancarditis.

Signs of endocarditis:

- Heart sounds are soft.
- PSM (due to MR).
- Mid-diastolic murmur (Carey Coomb's murmur).
- EDM (due to AR which is due to valvulitis with nodules on the valve).

Signs of myocarditis:

- Tachycardia.
- Soft heart sounds, S3 gallop.
- Cardiomegaly.
- Features of heart failure.

Signs of pericarditis:

- Pericardial rub (patient usually complains of chest pain).
- Pericardial effusion may be present.

Q: What is erythema marginatum?

A: It is characterized by transient raised pink or red rash, blanches on pressure, with clear centre and round margin. It occurs in 10% of cases, found mostly on the trunks and proximal limbs (but not on face). It may coalesce to form crescent or ring shaped patch.

Q: What is subcutaneous nodule?

A: These are small, firm and painless pea shaped nodules, felt over bony prominence and tendons or joints in extensor surface, present in 10 to 15% cases.

Q: What is Sydenham's chorea (St. Vitus' dance)?

A: It is a neurological manifestation of acute RF, usually occurs after 3 months of an acute attack, when almost all other signs disappear.

- Found in 1/3rd cases, common in children and adolescents, more in female of 5 to 15 years of age.
- Usually associated with emotional instability, irritability, inattentiveness and confusion.
- May occur without any other features of acute RF.
- Carditis is common, may be the first manifestation.
- Speech may be explosive and halting.
- ESR, ASO titre and CRP are usually normal.
- Relapse may occur only in few cases, occasionally during pregnancy (called chorea gravidarum) or in those who use oral contraceptive pill.
- Treatment—usually self-limiting, recovers within few months. Sedation (haloperidol) along with other treatment and prophylaxis of rheumatic fever should be given.

Q: How to treat acute RF?**A:** As follows:

1. Complete bed rest (until disease activity resolves).
2. Oral phenoxymethyl penicillin 250 mg 6 hourly for 10 days or single injection of benzathine penicillin 1.2 million units, deep IM in the buttock (to eliminate the streptococcal infection). Erythromycin may be given if allergic to penicillin.
3. Analgesic (to relieve pain): Aspirin 60 mg/kg per day in divided doses. Higher dose may be needed.
4. Other treatment:
 - For cardiac failure—diuretic, digoxin etc.
 - For pericarditis—NSAID, may be steroid in some case.
 - For carditis or severe arthritis: prednisolone 1 to 2 mg/kg daily.
 - For chorea: Diazepam for mild case and haloperidol in severe case.
5. Treatment of complications like cardiac failure, valvular lesion, heart block, arrhythmia etc. if needed.

Q: What is the prophylactic treatment of RF? How long it should be continued?**A:** Recurrence is common in patients who had carditis during initial episode. In children, 20% recurrence occurs within 5 years. Recurrence is uncommon after 5 years and in patients over 25 years of age.

To prevent recurrence:

- Oral phenoxymethyl penicillin 250 mg 12 hourly or injection benzathine penicillin 1.2 million units deep IM monthly should be given.
- In penicillin sensitive patients: erythromycin (250 mg 12 hourly) or clarithromycin may be used.
- Prophylactic drug should be continued up to 21 years of age or 5 years after the last attack (recurrence after 5 years is rare), whichever is longer.
- It should be extended if an attack has occurred in the last 5 years, if the patient lives in area of high prevalence or has a high exposure to streptococcal infection.
- If there is residual heart disease: Prophylactic should be continued for 10 years or 40 years of age, whichever is longer.
- If there is documented recurrence or documented rheumatic valvular heart disease: lifelong prophylaxis should be considered.

Q: What are the signs of activity in RF?**A:** Persistent fever, tachycardia, high ESR, leucocytosis and evidence of carditis.*N.B. Remember the following points:*

- *Skin infection with streptococci is not associated with RF.*
- *Streptococcal sore throat may not be present in some cases.*
- *More than 50% patients of RF with carditis will develop chronic valvular disease after usually 10 to 20 years.*
- *All the cardiac valves may be involved, but most commonly the mitral valve is affected (90%). Also aortic valve may be involved. Involvement of tricuspid and pulmonary valves are rare (5%).*
- *In chronic rheumatic heart disease, there is no history of RF in 50 to 60% cases.*
- *Arthritis is rheumatic fever that recovers completely without any residual change (rheumatic fever licks the joints, kills the heart).*

Q: What are the causes of migrating polyarthritis?

A: As follows:

- Rheumatic fever.
- Septicaemia.
- Gonococcal arthritis.
- Syphilitic arthritis.
- Lyme arthritis.
- Hyperlipidaemia (type II).
- SLE, sarcoidosis.
- Bacterial endocarditis.
- Whipple's disease.



Effusion in right knee in rheumatic fever



Swelling of knee joint in rheumatic fever

HYPERTROPHIC CARDIOMYOPATHY

Instruction by the examiner:

- Examine the CVS. Or, examine the pulse and precordium.

Presentation of a Case:

1. Pulse: 88/min, normal volume, normal in rhythm, no radio-femoral or radio-radial delay.
2. Carotid pulse: Jerky.
3. JVP: Normal ('a' wave may be prominent).
4. BP: 95/80 mmHg (low systolic, normal diastolic and narrow pulse pressure).
5. Precordium shows:
 - Apex beat is in left. . . intercostal space. . . cm from midline, heaving in nature (may be double apical impulse).
 - Systolic thrill is palpable at apex (or the lower left sternal border).
 - First and second heart sounds: Normal in all the areas.
 - Fourth heart sound may be present (due to atrial contraction).
 - There is a harsh ejection systolic murmur at the left lower sternal border and also a PSM at the apex.

My **differential diagnoses** are:

- Mitral regurgitation with aortic stenosis.
- Hypertrophic cardiomyopathy (HCM).

Q: What is the more **likely** diagnosis? Why?

A: HCM, because of double apical impulse and jerky carotid pulse.

Q: What are the factors that alter the **intensity** of the murmur at left lower sternal border?

A: It increases during standing and valsalva manoeuvre, decreases during squatting or sustained hand grip.

Q: Why **not** this is **purely AS**?

A: In AS, the findings are:

- Pulse is low volume and slow rising.
- BP shows low systolic, normal diastolic and narrow pulse pressure.
- Systolic thrill in aortic area.
- 2nd heart sound shows soft A2 in all the areas, P2 is normal, may be reversed splitting of 2nd heart sound.
- Harsh ejection systolic murmur in aortic area that radiates towards the neck.

Q: What **investigations** should be done in HCM?

A: As follows:

- X-ray chest (may be normal or cardiomegaly).
- ECG: may show LVH, infarction, deep T or bizarre pattern.
- Echocardiogram (diagnostic): shows asymmetric septal hypertrophy (ASH), systolic anterior motion of mitral valve (SAM).
- Cardiac MR.
- Genetic analysis.

READ THE FOLLOWING TOPICS IN RELATION TO CARDIOMYOPATHY

Q: What is **cardiomyopathy**? What are the **types**?

A: Cardiomyopathies are a group of disease that primarily affect the heart muscle and are not due to congenital, acquired valvular, hypertension, coronary arterial or pericardial abnormalities. 3 types:

- Dilated cardiomyopathy (ischaemic).
- HCM.
- Restrictive cardiomyopathy.

Q: What is **hypertrophic cardiomyopathy (HCM)**?

A: Hypertrophic cardiomyopathy is a disease of the heart muscle characterized by hypertrophy of cardiac muscle with malalignment of the cardiac fibres. Hypertrophy may be generalized or localized to the interventricular septum (asymmetrical septal hypertrophy) or other regions (apical HCM).

- It is a common type of cardiomyopathy. Prevalence is 1:500 to 1:1000, inherited as AD, but may be sporadic in 50% cases.
- In 50% cases, there is family history.
- Previously, it was called hypertrophic obstructive cardiomyopathy (HOCM), but no obstruction in most of the cases, left ventricular outflow obstruction is found only in 1/3rd patients.

Q: What is the **mechanism** of left ventricular outflow obstruction?

A: Asymmetric septal hypertrophy (ASH) and systolic anterior motion of mitral valve (SAM).

Q: What are the **types** of HCM?

A: As follows:

- Asymmetrical septal hypertrophy (70%).
- Basal septal hypertrophy (15 to 20%).
- Concentric (8 to 10%).
- Apical/lateral wall (<2%).

Q: What are the **presentations** of HCM? How **common** is the condition?

A: Patient may be asymptomatic. Detected on routine investigation.

Usual features are:

- Angina on effort.
- Dyspnoea on effort.
- Presyncope or syncope on effort.
- Sudden death may occur.

Overall prevalence is low, 0.2% of the population.

Q: What are the **complications** of HCM?

A: As follows:

- Sudden death.
- Atrial fibrillation.
- Ventricular arrhythmia.
- Infective endocarditis.
- Systemic embolism.
- Heart failure.

Q: What are the risk factors for sudden death in HCM?**A:** As follows:

- History of previous cardiac arrest or sustained VT.
- Recurrent syncope.
- Adverse genotype and/or family history of sudden cardiac death (<50 years old).
- Failure of BP to rise during exercise (no change or hypotension).
- Non-sustained VT on 24-hr Holter monitoring.
- Marked increase in left ventricular wall thickness (>30 mm on echocardiography).
- Delayed gadolinium enhancement on cardiac MRI.

Q: What are the markers of poor prognosis?**A:** As follows:

- History of syncope.
- Family history of sudden death.
- Non-sustained VT on 24-hr Holter monitoring.
- Marked increase in left ventricular wall thickness.
- Drop in BP during exercise.
- Particular genetic mutation.

Q: How to treat HCM?**A:** As follows:

1. In non-obstructive case:
 - Beta-blocker, rate limiting calcium channel blocker (e.g., verapamil, diltiazem) and disopyramide for symptomatic relief and prevention of syncope.
 - Amiodarone may be helpful in arrhythmia.
2. In significant left ventricular outflow obstruction:
 - Dual chamber pacing may be needed.
 - Outflow tract obstruction can be improved by partial surgical resection (myectomy).
 - Iatrogenic infarction of basal septum by injecting alcohol into one of the septal arteries with cardiac catheter (it is an alternative to surgical myomectomy).
3. Other treatment:
 - ICD (Implantable Cardioverter Defibrillator), if there is clinical risk factors for sudden death.
 - Cardiac transplantation may be needed in chronic heart failure (CHF) not responding to treatment.
 - Infective endocarditis prophylaxis may be needed.

Advice to the patient:

- Vigorous exercise and dehydration should be avoided.
- Genetic counselling, as in 50% cases it may be inherited as autosomal dominant.
- First degree family members should be screened by echocardiogram.

Q: What drugs should be **avoided** in HCM?

A: As follows:

- Digoxin.
- Vasodilators.
- Diuretics.
- Nitrates.
- Dihydropyridine calcium channel blockers.
- Alcohol (may cause vasodilatation).

Q: What is the effect of HCM in **pregnancy**? What **precautions** should be taken?

A: HCM is not a contraindication to pregnancy. The patient usually tolerates pregnancy well, if not severely symptomatic prior to conception. There is no evidence that pregnancy increases the risk of sudden cardiac death. Following precautions should be taken:

- Prenatal counselling regarding risk of disease in offspring.
- The patient should have regular follow up in well equipped centre with expertise in high risk pregnancies and cardiac disease.
- β -blocker or calcium channel blocker should be continued.

Q: What disease is **associated** with HCM?

A: Friedreich's ataxia.

RESPIRATORY
SYSTEM

3

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RESPIRATORY SYSTEM

3

'Work out the best method for examination, and practice it until it is a second nature to you'

INTRODUCTION

A case of respiratory system is usually selected in any clinical examination, either as a short case or long case. Also, it is an extremely common system tested in any oral examination, usually started with an X-ray or CT scan of chest. Usually examiner used to ask, 'Examine the chest'. However, many a times, examiner may ask to perform a particular part rather than the whole system and asks questions about that. For example:

- Examine the respiratory system.
- Examine the chest from front and/or back.
- Percuss and auscultate the chest. What are your findings?
- Auscultate the chest or put your stethoscope here. What are your findings?
- Percuss and auscultate the back of chest.

Common short cases:

- Obvious findings during inspection (e.g., tachypnoea, dyspnoea, lip pursing and thoracic deformity). Puffy, plethoric face with congested eyes (superior vena caval obstruction).
- Pleural effusion (unilateral or bilateral).
- Bronchiectasis (unilateral or bilateral).
- Consolidation.
- Collapse of the lung.
- DPLD (previously called interstitial lung disease or fibrosing alveolitis).
- Emphysema.
- COPD.
- Pneumothorax.

During examination of the patient, examiner may interrupt at any step and ask questions, for example:

- What is **vocal fremitus**? What are the **causes** of increased or decreased vocal fremitus?
- What is the **percussion** note? Supposing it is dull, what are the **causes** of dullness on percussion?
- What are your **findings** on auscultation? Supposing bronchial sound, what are the **causes** of bronchial sound?

So, during examination, you must be ready to answer any questions. After completing the clinical examination, one should present the case according to the examiner's instruction. For example:

- Present your case or what are your **findings?** (Mention systematically in the form of **inspection, palpation, percussion and auscultation**).
- Have you finished? What is your **diagnosis?** (Yes, I have finished my examination. Diagnosis is right sided pleural effusion). Why it is pleural effusion? (Because Mention the signs of pleural effusion systematically).

If you are asked to examine the back of chest only, tell the patient to keep both hands on the shoulder, i.e., right hand on left shoulder and the left on right. Look for clubbing, any change of joints (rheumatoid arthritis), skin change (systemic sclerosis, dermatomyositis), a good clue for the diagnosis, may be associated with DPLD. If there is clubbing with bilateral basal creps, it may be due to bronchiectasis, DPLD etc.

Remember, common symptoms of any respiratory diseases are:

- Cough with or without sputum production.
- Breathlessness.
- Haemoptysis.
- Chest pain.
- Wheezing.
- Runny or blocked nose.
- Sneezing etc.

Also, other related symptoms are—Heaviness or compression of the chest, hoarseness of voice, weight loss (related to TB or bronchial carcinoma), syncopal attack (cough syncope), fever, sleep disturbance, swelling of legs (in chronic cor pulmonale).

EXAMINATION ROUTINE

Proceed as follows:

- Introduce yourself, 'Good morning, I am Dr. . . . I would like to examine your chest. Would you please allow me to do so? Please tell me if I hurt you or if you feel any discomfort'.
- Undress the patient up to the waist with permission (be careful in case of a female patient). The patient should lie flat, but if acutely ill or dyspnoeic, he/she can be examined in the position in which the patient feels comfortable.

If you are asked to examine the respiratory system, the following important **general examinations** should be done:

1. While talking, hoarseness of voice (indicates laryngitis or recurrent laryngeal nerve palsy).
2. Dyspnoeic, orthopnoeic or tachypnoeic (count the respiratory rate).
3. Cough with wheeze (due to bronchial asthma, chronic bronchitis, COPD) or stridor (due to large airway obstruction).
4. Prominent accessory muscles of respiration (indicates COPD).
5. Lip pursing (in emphysema).

6. Cyanosis.
7. Cachexic or emaciated (due to tuberculosis, bronchial carcinoma, lean and thin in emphysema), obesity (associated with sleep apnoea syndrome).
8. Engorged and pulsatile neck veins (due to cor pulmonale) or engorged non-pulsatile veins in SVC obstruction.
9. In the face (look at the following points carefully):
 - Pink puffer (due to emphysema).
 - Blue bloater (due to chronic bronchitis).
 - Puffy, oedematous, plethoric and red eyes (due to SVC obstruction).
 - Cushingoid face (may be due to prolonged use of steroid in bronchial asthma or COPD).
 - Skin change (in systemic sclerosis, may cause DPLD).
 - Butterfly rash (due to SLE or dermatomyositis).
 - Eye with Horner's syndrome (in which there is partial ptosis, constricted pupil) in Pancoast's tumour.
10. In the hands (look at the following points carefully):
 - Nicotine staining in nails (may be associated with bronchial carcinoma).
 - Clubbing.
 - Cyanosis.
 - Wasting (due to involvement of lower trunk of brachial plexus by bronchial carcinoma, C8 and T1 lesions).
 - Pulse: Tachycardia, pulsus paradoxus (due to severe obstructive airway disease), high volume and bounding pulse (due to CO₂ excess).
 - Warm and sweaty hands (due to anoxic cor-pulmonale).
 - Flapping tremor (due to severe respiratory failure and CO₂ retention).
 - Signs of other diseases such as joint deformity in rheumatoid arthritis, skin change in systemic sclerosis or dermatomyositis (which may cause DPLD).
11. In the legs:
 - Oedema (due to cor-pulmonale).
 - Deep vein thrombosis (which can cause pulmonary embolism).
 - Clubbing and cyanosis.
12. Heart (to see evidence of pulmonary hypertension, features of mitral stenosis, which causes pulmonary oedema, signs of chronic cor-pulmonale etc.).
13. In the abdomen:
 - Liver (may be enlarged and tender in cor-pulmonale with CCF).
 - Paradoxical inward motion of abdomen during inspiration (which indicates diaphragmatic paralysis).
14. Lymph nodes (may be due to lymphoma, metastasis, TB and sarcoidosis), which can involve the lung.

EXAMINATION OF THE CHEST

(Examine systematically: **Inspection, palpation, percussion** and **auscultation**. Also present the case in the same way. Always examine both front and back of chest, both right and left side during each part of examination.)

Inspection:

- Shape of chest (asymmetry or deformity such as kyphoscoliosis, pectus excavatum or carinatum), flattening, drooping of the shoulder (due to fibrosis or collapse).
- Movement of chest (unilateral or bilateral restriction), movement upward (in emphysema).
- Intercostal space (any fullness, indrawing of lower ribs).
- Scar marks (thoracotomy scar, thoracoplasty).
- Radiation marks.
- Visible impulse (cardiac impulse, epigastric pulsation).
- Visible, engorged vein in chest (in SVC obstruction).
- Others: Suprasternal and supraclavicular excavation (indicates hyperinflation of lungs), prominent accessory muscles, gynaecomastia, needle puncture mark (due to pleural aspiration) or tattoo marking.

Palpation:

- Position of trachea (whether it is central, deviated to right or left).
- Apex beat.
- Vocal fremitus.
- Chest expansion (always measure by measuring tape in full inspiration).
- Tracheal tug (descent of trachea during inspiration. Examine by placing fingers over the trachea. Presence of tracheal tug indicates hyperinflation).
- Crico-sternal distance (it is the distance between suprasternal notch and cricoid cartilage. Normally, 3 fingers or more. If it is less, indicates hyperinflation).
- Rib tenderness (due to trauma or fracture, secondary deposit).
- Tenderness in costochondral junction (due to Tietze syndrome).
- Others—palpable pleural rub, crepitus sound (due to subcutaneous emphysema).

Percussion:

- Percussion note (normal resonance, hyperresonance, stony dull or woody dull, impaired dullness).
- Area of liver dullness (normally in the right 6th rib or 5th intercostal space in mid-clavicular line. It is obliterated or lower down in emphysema or severe asthma).
- Area of cardiac dullness (obliterated due to emphysema or severe asthma).

Auscultation:

Turn the head of the patient to the left side and tell him, 'Keep your mouth open, take deep breath in and out for me'. Place the stethoscope, check both right and left side alternately.

1. Breath sound (normal vesicular, vesicular with prolonged expiration or bronchial).
2. Vocal resonance (normal, increased, decreased or absent). If the vocal resonance is increased, always test for whispering pectoriloquy (usually it is present).
3. Added sounds:
 - Rhonchi (high or low pitched, localized or generalized).
 - Pleural rub.
 - Crepitations (fine or coarse or end inspiratory. If crepitations are present, ask the patient to cough and see again).
 - Post-tussive crepitations (appear after cough), found due to TB.
 - Succussion splash (may be found in hydropneumothorax), see in selected case if suspected.

N.B.: Remember the following points:

- *After completing the examination in front, ask the patient to sit, then examine back of chest systematically, in the same way like inspection, palpation, percussion, auscultation.*
- *Carefully, auscultate the lung bases to see basal crepitations.*

Finally, see the following points:

- If the diagnosis is COPD, see forced expiratory time (FET) by asking the patient to exhale forcefully after full inspiration, while you listen by placing your stethoscope over the trachea.
- Normally, it is <6 s, if >6 s, it indicates airway obstruction.
- If any sputum cup is available nearby, look at the sputum and comment on it.

READ THE FOLLOWING ABOUT SOME FINDINGS IN ROUTINE EXAMINATION INSPECTION:

Respiratory Rate:

- Normally, it is 14 to 18/min (in adult).
- Increased rate of respiration is called tachypnoea (>20). Usually, it is faster in children, slower in the elderly.
- Increased depth of respiration is called hyperpnoea.

Causes of **tachypnoea** (increased rate of respiration):

1. Physiological: Anxiety, fear, exercise or exertion.
2. Pathological:
 - Respiratory causes: bronchial asthma, pneumonia or other respiratory infections, pulmonary embolism, COPD.
 - Cardiac causes: acute anterior myocardial infarction, acute left ventricular failure.
 - Others: Fever, metabolic acidosis (diabetic ketoacidosis, lactic acidosis and renal failure), hysterical conversion reaction (HCR) and cerebrovascular disease (CVD).

Causes of **reduced** respiratory rate:

- Sleep.
- Depression of respiratory centre (by narcotic drugs such as morphine, in some CVD).

N.B.: Remember the following points:

- *Normally, respiration in male is abdomino-thoracic (as man uses diaphragm more than intercostal muscles).*
- *Respiration in female is thoraco-abdominal (as woman uses intercostal muscles more than diaphragm). In babies, it is abdominal (diaphragmatic).*
- *If respiratory movement is **exclusively abdominal**, think of the following causes: Ankylosing spondylitis, intercostal muscle paralysis, pleuritic pain or any painful condition of chest.*
- *If respiratory movement is **exclusively thoracic**, it indicates reduced diaphragmatic movement due to peritonitis, ascites and pregnancy.*

Abnormal Breathing:

1. **Kussmaul's breathing (air hunger):** It is characterized by deep, sighing, rapid respiration at regular rate due to stimulation of respiratory centre. Causes are (due to metabolic acidosis):
 - Diabetic ketoacidosis.
 - Renal failure.
 - Occasionally in severe respiratory failure and hepatic failure.
2. **Ataxic breathing (Biot breathing):** Characterized by irregular respiration in timing and depth. It indicates brain stem damage (due to CVA and head injury).
3. **Cheyne–Stokes breathing:** Cyclical variation in the depth of respiration characterized by gradual deepening of respiration till a maximum is attained, followed by gradual diminished respiration till a period of apnoea occurs (apnoea alternates with hyperpnoea). It is due to diminished sensitivity of respiratory centre to CO₂. The cycle may last for 2 min. Causes are:
 - Acute LVF (or severe heart failure).
 - Coma due to any cause.
 - Brain damage due to head injury and cerebral haemorrhage.
 - Narcotic drug poisoning.
 - Sometimes, at high altitude.
4. **Apneustic breathing:** Characterized by a post-inspiratory pause in breathing. It indicates pontine damage.
5. **Paradoxical breathing:** If abdomen sucks inward during inspiration. It indicates diaphragmatic paralysis.

Shape of the Chest (Deformity or Asymmetry):

1. **Asymmetry:** Whether any kyphosis, scoliosis, lordosis, flattening of chest.
2. **Pigeon chest (pectus carinatum):** It is localized prominence, outward bowing of sternum and costal cartilage. Causes are:
 - Congenital.
 - Ricket.
 - Marfan's syndrome.
 - Homocystinuria.
 - Repeated respiratory infection in childhood (causing strong diaphragmatic contraction as the thorax remains pliable).
 - Bronchial asthma since childhood.
 - Osteogenesis imperfecta.
3. **Pectus excavatum** (funnel chest, saucer or cup): It is the localized depression at the lower end of sternum or rarely depression of whole length of the body of sternum and of costal cartilage attached to it. It does not usually cause any problem. Rarely, it may cause lung and cardiac problems (pulmonary hypertension and cor pulmonale). Causes are:
 - Congenital (common cause).
 - Ricket.
 - Marfan's syndrome.
 - Homocystinuria.
 - Osteogenesis imperfecta.



Pectus carinatum



Pectus excavatum



Harrison sulcus

4. **Harrison sulcus:** It is a groove directed outward and slightly downward from the sternum in the lower part of the chest anteriorly, along the line of attachment of diaphragm (due to indrawing of ribs). Causes are:

- Chronic bronchial asthma since childhood.
- Ricket.



Barrel-shaped chest



Rickety rosary



Kyphoscoliosis

5. **Barrel-shaped chest:** Antero-posterior diameter of the chest is increased than the transverse diameter, ribs look more horizontal, intercostal spaces appear full, chest remains like full inspiration, subcostal angle $>90^\circ$ (normally 90° or less). It is detected by placing two hard boards, one on the front and another on the back of the chest and measure the distance between these two for antero-posterior diameter (normal ratio of A:P diameter is 5:7). Causes are:
- Emphysema.
 - Severe chronic asthma.
6. **Rickety rosary:** It is the prominent swelling at the costo-chondral junction due to rickets.
7. **Flail chest:** It occurs in multiple fractures of ribs and sternum. There is paradoxical inward movement of chest during inspiration.
8. **Thoracoplasty:** In this procedure, some ribs are resected on one side of the chest to achieve permanent collapse of the lung. Usually one side of the upper part of the chest is depressed. Previously, it was done to treat pulmonary tuberculosis (before the development of chemotherapy).

Reduction of Movement of Chest:

Any respiratory disease is associated with reduction or restricted movement of chest on the affected side. Causes are:

1. Unilateral:
 - Pleural effusion.
 - Pneumothorax.

- Collapse.
- Fibrosis.
- Consolidation.

2. Bilateral:

- COPD (especially in emphysema).
- Diffuse bilateral pulmonary fibrosis.

PALPATION:

Expansion of the Chest:

It is measured by placing the hands in lower part of the chest (also in middle part), fingers are placed on the side of chest keeping the thumbs in midline and close to each other (can also be measured using tape at the level of nipple). Ask the patient to take deep breath in and out. Normal expansion is >5 cm.

Causes of **reduced** expansibility:

- Emphysema (in severe emphysema, it is <1 cm).
- Pleurisy.
- Ankylosing spondylitis.
- Respiratory muscle paralysis.

Trachea:

Normally, it is slightly deviated to the right. Causes of **shifting** of trachea:

1. Same side (on the side of lesion):

- Collapse.
- Fibrosis.
- Pneumonectomy.
- Agenesis of one lung.

2. Opposite side (opposite to the side of lesion):

- Pleural effusion.
- Pneumothorax.

Apex Beat:

May be shifted, causes are as in trachea (see above). Apex beat is also shifted in kyphoscoliosis, pectus excavatum and cardiac cause.

N.B.: Remember the following points:

- *Trachea may be shifted in retrosternal goitre.*
- *Level of tracheal bifurcation: At the lower end of manubrium sterni (angle of Louis) in front and in the back, between fourth and fifth thoracic vertebrae.*
- *Shifting of apex beat and trachea indicates mediastinal shifting.*
- *Sometimes, these may not be shifted, if mediastinum is fixed (causes of fixed mediastinum are fibrosing mediastinitis, radiotherapy or methysergide therapy, traumatic, idiopathic).*

Vocal Fremitus:

May be normal, or increased or decreased (it is less practiced now a day, as vocal resonance is seen, which is more sensitive).

Causes of increased vocal fremitus (3 C's):

- Consolidation.
- Collapse with patent bronchus.
- Cavity (large).
- Also in fibrosis.

Causes of decreased vocal fremitus:

- Pleural effusion.
- Thickened pleura.
- Pneumothorax.
- Collapse with complete bronchial obstruction.
- Mass lesion (bronchial carcinoma, hydatid cyst).

Percussion:

Percussion note may be normal resonance, hyper-resonance, dull or stony dull or impaired dullness.

Causes of hyper-resonance:

- Pneumothorax.
- Big cavity.
- Big bullae.
- Emphysema (usually increase resonance).

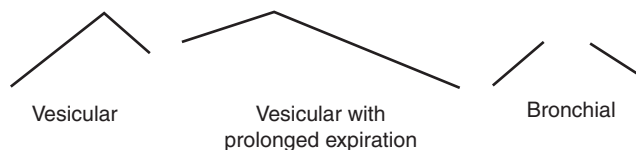
Causes of dullness:

- Pleural effusion (stony dull).
- Thickened pleura (impaired dull).
- Consolidation (woody dull).
- Collapse.
- Mass lesion.
- Raised diaphragm due to hepatomegaly (dullness on the right side).

AUSCULTATION:

Breath sound: It should be heard using the diaphragm of stethoscope, compare both sides. Use the bell above the clavicle to hear lung apices. Breath sound may be normal (vesicular), bronchial, vesicular with prolonged expiration, diminished or absent.

- 1. Normal vesicular** (similar to wind rustling in leaves): It is louder and longer in inspiration and expiration is short, without any gap. Vesicular sound is produced in large airways. When heard through normal lung, filtering effect through the alveoli produces attenuated and low pitched sound.



2. Bronchial: Harsh, louder, blowing quality, inspiration and expiration are of equal length and intensity. There is a gap between inspiration and expiration. It is produced in large airways, but when the lung between airway and chest wall is airless (e.g., consolidation), loss of filtration effect results in high pitched bronchial sound. It is 2 types:

- High pitched (tubular): Found in consolidation and collapse with patent bronchus.
- Low pitched (also called cavernous): Found in cavitation.

Causes of bronchial sound (3 C's):

- Consolidation.
- Collapse with patent bronchus.
- Cavity (near the chest wall).
- Also fibrosis (low pitched).

3. Causes of vesicular with prolonged expiration:

- COPD (chronic bronchitis and emphysema).
- Bronchial asthma.

Vocal Resonance:

This may be normal, increased or decreased. Vocal resonances are 3 types:

- Bronchophony: It appears to be near the ear piece, found in consolidation.
- Aegophony: Nasal quality or goat like (Greek: *aix* means goat and *phony* means sound), found in consolidation and above the fluid level of pleural effusion.
- Whispering pectoriloquy: Ask the patient to tell '**ninety-nine**' or '**one-one**', as if whisper. When auscultated with stethoscope, it appears as if the patient whispers in the examiner's ear. It may be found in consolidation, collapse with patent bronchus or cavitation (3 C's).

N.B.: If bronchial sound is present, whispering pectoriloquy is also present. Hence, always auscultate for whispering pectoriloquy.

Causes of increased vocal resonance (3 C's):

- Consolidation.
- Collapse with patent bronchus.
- Cavity.
- Also in fibrosis.

Causes of decreased vocal resonance:

- Pleural effusion.
- Thickened pleura.
- Pneumothorax.
- Collapse with complete bronchial obstruction.
- Mass lesion.

Added Sounds:

- Pleural rub.
- Crepitations.
- Rhonchi.

Pleural Rub:

- It is the localized grating, creaking, rubbing and leathery sound produced by movement of visceral pleura over the parietal pleura.
- Heard both in inspiration and expiration, disappears when breathing is hold (to differentiate from pericardial rub).
- Rub is augmented by pressing the stethoscope.
- May be palpable and associated with local pain.

Presence of pleural rub indicates pleurisy (which may be due to viral or other infections, pneumonia, pulmonary infarction and bronchial carcinoma).

Pleuro-pericardial rub:

- When pleurisy involves the pleura adjacent to pericardium, pleura-pericardial rub is heard (there is no pericarditis).
- It is due to rough pleural surface adjacent to pericardium, which moves one upon another by cardiac pulsation.

Q: What are the **differences** between pleural rub and pericardial rub?

A: As follows:

Pleural Rub	Pericardial Rub
1. Anywhere on chest.	1. Over precordium, but better in left lower parasternal area (bare area of the heart).
2. Absent, if respiration is stopped.	2. No relation with respiration.
3. It is due to pleurisy.	3. It is due to pericarditis.

Creptitations:

These are bubbling or crackling sounds, occur due to passage of air through fluid in alveoli. Creptitations may be fine or coarse, may be present in inspiration, expiration or both.

- Early inspiratory creptitations: commonly found in chronic bronchitis.
- End or pan-inspiratory creptitations: found in fibrosing alveolitis (DPLD).

Causes of **coarse creptitations** (see also page 272):

- Bronchiectasis (may be unilateral or bilateral).
- Resolution stage of pneumonia.
- DPLD (or ILD).

Creptitations **reduce** or **disappear** after coughing in the following diseases:

- Resolving pneumonia.
- Bronchiectasis.
- Lung abscess.
- Pulmonary oedema.

Creptitation **not changed** after coughing: Found in DPLD.

Causes of **bilateral basal crepitations**:

- Bilateral bronchiectasis.
- Pulmonary oedema due to any cause (commonly acute LVF).
- DPLD.

Q: Why **end-inspiratory** coarse crepitation in DPLD?

A: It is due to reopening of collapsed alveoli at the end of inspiration (not due to fluid in alveoli).

Q: What are the **differences** between pleural rub and crepitation?

A: As follows:

Pleural Rub	Crepitations
1. It is grating or creaking or rubbing sound	1. Bubbling or crackling sound
2. No change with cough	2. Changes with cough
3. It may be palpable	3. Not palpable
4. Augmented by pressing stethoscope	4. Not so
5. Local pain due to pleurisy	5. No local pain

Rhonchi:

It is the musical sound produced by passage of air through narrow airways (due to mucosal oedema or spasm of bronchial musculature). It is 2 **types**:

- High pitched: Indicates small airway obstruction.
- Low pitched: Indicates large bronchi obstruction.

Causes of rhonchi:

- Bronchial asthma (medium or high pitched, more in expiration).
- Chronic bronchitis (low or medium pitched, both in inspiration and expiration).

Localized rhonchi (indicates partial obstruction of large bronchus). Usually a fixed, low pitched rhonchi. Causes are:

- Neoplasm (bronchial carcinoma, adenoma).
- Foreign body.
- Mucous plugs (disappear after coughing).
- Congenital bronchial stenosis.

Bedside Lung Function Tests:

- **FET** (forced expiratory time): Ask the patient to exhale forcefully after full inspiration while you listen by placing your stethoscope over the trachea. Normally, patient can empty in <6 s. If >6 s, indicates airway obstruction (remember the age, add 1 s for every decade, e.g., a 40 year old person can exhale in 4 s).
- **PEFR** (peak expiratory flow rate): Done using Wright peak flow meter. Normally in young males, it is 600 L/min, in female, 400 L/min (value varies with age, sex and height. Table for the normal value should be seen). It is reduced in COPD and bronchial asthma.

DRUG INDUCED LUNG DISEASE

1. Drugs that cause or aggravate bronchial asthma:

- β -Blockers.
- Aspirin and other NSAIDs.
- Tamoxifen.
- Dipyridamole.
- Nebulized pentamidine: used for the treatment of *Pneumocystis carinii* (*Pneumocystis jiroveci*) infection.

2. Drugs that cause cough:

- ACE inhibitors (e.g., Lisinopril, ramipril. More in females, actual mechanism is unknown). This drug causes conversion of angiotensin-1 to angiotensin-2. Also, causes breakdown of bradykinin and substance P. All these may cause cough.

3. DPLD (non-eosinophilic alveolitis):

- Busulphan.
- Bleomycin.
- Methotrexate.
- Amiodarone.
- Nitrofurantoin.
- Azathioprine.

4. Pulmonary eosinophilia:

- Antibiotics (sulphonamide, penicillin, tetracycline, nitrofurantoin).
- Anti-rheumatic agent (gold, aspirin, penicillamine, naproxen).
- Anti-convulsant (phenytoin, carbamazepine).
- Anti-depressant or antipsychotic (imipramine, chlorpromazine, dothiepin).
- Cytotoxic (methotrexate, bleomycin, procarbazine).

5. Adult respiratory distress syndrome (ARDS):

- Aspirin and opium (in overdose).
- Streptokinase.
- Hydrochlorothiazide.

6. Pleural disease or effusion:

- Bromocriptine.
- Nitrofurantoin.
- Methotrexate.
- Methysergide.
- By SLE (hydralazine, INH, procainamide, phenytoin, carbamazepine, chlorpromazine).

7. Mediastinal widening or hilar lymphadenopathy (pseudolymphoma):

- Phenytoin or diphenylhydantoin.

8. Respiratory failure:

- Opium.
- Sedative or hypnotic.
- Alcohol.
- Tricyclic antidepressant.

Q: What is dyspnoea?

A: It is the unpleasant, subjective awareness of breathing.

Causes of **acute or sudden dyspnoea:**

- Acute severe asthma.
- Pulmonary oedema (acute LVF).
- Pulmonary embolism.
- Spontaneous pneumothorax.
- Adult respiratory distress syndrome.
- Hysterical conversion reaction or panic attack.

Cause of **dyspnoea on supine:** Phrenic nerve palsy (bilateral diaphragmatic paralysis).

Platypnoea: It means dyspnoea that worsens on upright position. It occurs in arteriovenous malformation at lung bases resulting in increased shunting and hypoxia in upright position.

PLEURAL RUB OR CREPITATIONS

Instruction by the examiner:

- Put your stethoscope here (on chest). What is your finding?

Presentation of a Case 1:

- There is pleural rub (tell the site).

Q: Describe pleural rub.

A: It is a localized scratchy, grating, cracking, rubbing or leathery sound produced by movement of visceral pleura over parietal pleura, augmented by pressing the stethoscope. It is present both in inspiration and expiration and disappears when breathing is stopped. It may be palpable and associated with local pain.

Q: What does it indicate?

A: Pleurisy.

Q: What are the causes of pleurisy?

A: It may be due to viral (commonly coxsackie B) or other infections, pneumonia, pulmonary infarction and bronchial carcinoma.

Q: What is patient's complaint or, how the patient presents?

A: Pleuritic chest pain.

Q: What are the characteristics of pleuritic chest pain?

A: It is characterized by sharp, localized, lancinating chest pain, which is aggravated by coughing, deep breathing, change of posture and movement.

Q: What is the differential diagnosis of pleural rub? How to differentiate?

A: Crepitations. (For differentiation, see in the previous discussion).

Presentation of a Case 2:

- There are multiple crepitations (mention fine or coarse) present in both inspiration and expiration (mention whether unilateral or bilateral, and the site).

Q: What do you think are the causes of crepitations?

A: Mention whether it is unilateral or bilateral:

If **unilateral**, causes are:

- Unilateral bronchiectasis.
- Resolution stage of pneumonia.
- Lung abscess.

If **bilateral**, causes are:

- Bilateral bronchiectasis.
- Pulmonary oedema.
- DPLD.

Q: What is crepitation?

A: These are bubbling or crackling sounds that occur due to passage of air through fluid in alveoli. Crepitations may be fine or coarse, present in inspiration, expiration or both.

Q: How to **differentiate** between pleural rub and crepitation?

A: See in the previous discussion.

Q: What are the **differences** between pleural rub and pericardial rub?

A: See in the previous discussion.

PLEURAL EFFUSION

Instruction by the examiner:

- Examine the chest for respiratory system or, examine the back of the chest.
- Percuss and auscultate the back of the chest.

N.B.: Before examining, see any needle puncture mark, local dressing with gauze and tape, any scar mark, and mention it.

Presentation of a Case: (Supposing Right Sided, Tell the Findings in Right Side).

On inspection:

- Restricted movement (there is one puncture mark, gauze and tape, mention if any).

On palpation:

- Trachea and apex beat: Shifted to the left side.
- Vocal fremitus: Reduced or absent in right side (up to . . ., mention the location).
- Chest expansion is reduced.

On percussion:

- Stony dullness (up to . . ., mention the location).

On auscultation:

- Breath sound: Diminished or absent (mention the location).
- Vocal resonance: Diminished or absent (mention the location).
- No added sound.

My diagnosis is **Right sided pleural effusion.**

Q: What are the **differential diagnoses?**

A: As follows:

- Thickened pleura.
- Mass lesion.

Q: Why this is not **thickened pleura?**

A: In thickened pleura, no mediastinal shifting and dullness is impaired (not stony).

Q: Why not this is **consolidation?**

A: In consolidation, dullness is woody, no shifting of mediastinum, breath sound is bronchial and vocal resonance is increased.

Q: Why not this is **collapse?**

A: In collapse, apex beat and trachea will be shifted to the same side (also, in collapse with patent bronchus, there is bronchial breath sound and increase vocal resonance).

Q: Why not **pneumothorax?**

A: In pneumothorax, there is hyperresonance on percussion.

Q: What are the **possible** findings just above the effusion?

A: As follows:

- Bronchial sound.
- Increased vocal resonance.
- Whispering pectoriloquy.
- Pleural rub.

(These findings are due to compression collapse of lung).

Q: What is **pleural effusion**?

A: Accumulation of excessive amount of fluid in pleural cavity is called pleural effusion.

Q: Can there be **chest pain** in pleural effusion?

A: Chest pain may occur due to pleurisy (may be present in mild effusion).

Q: What are the causes of **dullness on percussion** over lower chest?

A: As follows:

- Pleural effusion (stony dullness).
- Thickened pleura.
- Consolidation (woody dullness).
- Collapse of the lung.
- Raised right hemidiaphragm (due to hepatomegaly or liver pushed up).
- Mass lesion.

Q: What are the **definitive signs** of pleural effusion?

A: Stony dullness and reduced or absent breath sound (confirm by aspiration).

Q: What are **causes** of pleural effusion in this case?

A: Mention the causes considering the age and sex:

If the patient is young, the causes are:

- Common causes: Pulmonary tuberculosis and parapneumonic.
- Others: Lymphoma and SLE in female (also pulmonary infarction).

If the patient is middleaged or elderly, the causes are:

- Pulmonary tuberculosis.
- Parapneumonic.
- Bronchial carcinoma.

Four common causes of pleural effusion:

- Pulmonary tuberculosis.
- Parapneumonic.
- Bronchial carcinoma.
- Pulmonary infarction.

N.B.: Remember the following points in pleural effusion:

- Pleural fluid normally present: 5 to 15 mL.
- At least, 500 mL of fluid is necessary to detect clinically.
- At least, 200 mL of fluid is necessary to detect radiologically in PA view.
- At least, 100 mL of fluid is necessary to detect radiologically in lateral decubitus position.
- Less than 100 mL or small amount of fluid is detected by ultrasonography (even 20 to 25 mL fluid can be detected).

Q: How to **confirm** if there is small effusion? (If not detected by chest X-ray PA view.)

A: By doing:

- X-ray in lateral decubitus position.
- Ultrasonogram of lower part of the chest.
- Occasionally, CT scan of chest may be needed.

Q: If **clinically** pleural effusion, but there is **no fluid** during aspiration, what are the **possibilities**?

A: As follows:

- Thickened pleura.
- Fluid may be thick (empyema).
- Mass lesion.

Q: What are the causes of predominantly **right** or **left sided** pleural effusion?

A: As follows:

Causes of right sided pleural effusion:

- Liver abscess.
- Meig's syndrome.
- Dengue haemorrhagic fever.

Causes of left sided pleural effusion:

- Acute pancreatitis.
- Rheumatoid arthritis.
- Dressler's syndrome.
- Oesophageal rupture (Boerhaave syndrome).
- Dissecting aneurysm.

Q: What are the **types** of pleural effusion according to the colour?

A: According to colour, pleural effusion may be:

- Serous (hydrothorax).
- Straw.
- Purulent (empyema or pyothorax).
- Haemorrhagic (haemothorax).
- Milky or chylous (chylothorax).



Haemorrhagic



Straw colour



Serous



Chylous

***N.B.:** Clinically, only pleural effusion should be mentioned. After drawing the fluid and according to its colour, other diagnosis may be done, e.g., if pus, it is empyema.*

Q: What **relevant findings** should be seen to find out the **cause** of pleural effusion?

A: As follows:

- Oedema: Due to hypoalbuminaemia, nephrotic syndrome.
- Emaciation: Due to TB, malignancy.
- Malnutrition: May cause hypoalbuminaemia.
- Lymph node: Due to lymphoma.
- Clubbing, nicotine stain, radiation mark: Due to bronchial carcinoma.
- Signs of rheumatoid arthritis, SLE.
- Stigmata of CLD.
- Signs of CCF.
- Signs of myxoedema.

Q: What **investigations** should be done in pleural effusion?

A: Mention according to the age of patient and suspected cause:

1. Chest X-ray PA view (if small effusion, lateral decubitus view).
2. CBC with ESR (high ESR in TB, leucocytosis in pneumonia).
3. Mantoux test (MT).
4. Aspiration of fluid for analysis:
 - Physical appearance (straw coloured, serous, haemorrhagic, chylous).
 - Gram staining, cytology (routine) and exfoliative cytology (malignant cells).
 - Biochemistry (protein and sugar). Also simultaneous blood sugar, protein and LDH may be done.
 - Adenosine deaminase (ADA, high in tuberculosis).
 - C/S.
 - AFB (in some cases, mycobacterial C/S).
5. Others (of pleural fluid), according to suspicion of causes:
 - Cholesterol, LDH and rheumatoid factor (in RA).
 - Amylase (high in acute pancreatitis, oesophageal rupture and malignancy).
 - Triglyceride (in chylothorax).
6. Pleural biopsy by Abram's or Cope needle (positive in 80% cases with TB and 40 to 60% cases with bronchial carcinoma).
7. Other investigations according to suspicion of causes:
 - ANA, anti-ds DNA (in SLE).
 - Liver function tests (in CLD).
 - Urine for protein and serum total protein, Albumin:globulin ratio (in nephrotic syndrome).
 - If palpable lymph node: FNAC or biopsy (for lymphoma, metastasis).
8. CT scan in some cases.

Q: What is the role of **pleural fluid amylase**?

A: Pleural fluid amylase may be higher than serum amylase in acute pancreatitis, bacterial pneumonia, oesophageal rupture and malignancy. It is high in adenocarcinoma of lung and may be useful in differentiating from mesothelioma.

Q: What are the causes of **high eosinophil** in the pleural fluid (also high in the blood)?

A: Pulmonary eosinophilia, polyarteritis nodosa and rarely lymphoedema (high eosinophil in pleural fluid, but not in blood is likely due to pulmonary embolism. High eosinophil in pleural fluid is unlikely to be malignant).

Q: How to differentiate between exudative and transudative pleural effusion?

A: As follows:

Criteria	Exudative	Transudative
1. Appearance	Straw, purulent, hazy, chylus or blood stained.	Clear or serous.
2. Protein	>3 gm%.	<3 gm%.
3. Glucose	Low.	Normal.
4. Cholesterol	>60 mg/dl.	<60 mg/dl.
5. LDH	Greater than 2/3 rd of the upper limit of normal serum LDH.	Less than 2/3 rd of the upper limit of normal serum LDH.
6. Pleural fluid LDH: Serum LDH	>0.6.	<0.6.
7. Pleural fluid protein: Serum protein	>0.5.	<0.5.
8. Serum-effusion albumin gradient (serum albumin – pleural fluid albumin)	<1.2 gm/dl.	>1.2 gm/dl.

N.B.: Remember the following:

- Pleural fluid cholesterol level <60 mg/dl indicates transudate. In all malignant effusion, pleural fluid cholesterol > 60 mg/dl.
- High pleural fluid ADA indicates tubercular pleural effusion.

READ THE FOLLOWING TOPICS IN RELATION TO PLEURAL EFFUSION

Causes of pleural effusion: 2 types—**Exudative** and **transudative**.

1. Exudative (protein >3 gm%):

- Pulmonary TB.
- Pneumonia.
- Bronchial carcinoma.
- Pulmonary infarction.
- Collagen diseases (SLE and RA).
- Lymphoma.
- Dressler's syndrome (post myocardial infarction syndrome characterized by pain, pyrexia, pericarditis, pleurisy and pneumonitis).
- Others (acute pancreatitis, subphrenic abscess, liver abscess, pleural mesothelioma, secondaries and yellow nail syndrome).

2. Transudative (protein <3 gm%):

- Congestive cardiac failure.
- Nephrotic syndrome.
- Cirrhosis of liver.
- Malnutrition.
- Hypothyroidism.
- Meig's syndrome (characterized by ovarian fibroma, ascites and right sided pleural effusion).
- Chronic constrictive pericarditis.
- Acute rheumatic fever.

Q: What is pseudotumour (phantom tumour)?

A: It is the accumulation of fluid in interlobular fissure, usually found along the lateral chest wall. Chest X-ray shows rounded homogeneous opacity, looks like localized or encysted effusion, misdiagnosed as tumour. It is confirmed by ultrasonography or CT scan. It disappears with resolution of effusion. Commonly found in CCF.

Q: What is yellow nail syndrome?

A: It is a congenital disorder characterized by:

- Nails: Yellow, thick, onycholysis.
- Lymphoedema of legs.
- Pleural effusion or bronchiectasis.

Q: What are the features of parapneumonic effusion? How to treat?

A: Usually small and localized, may be noninfected or infected fluid. Any loculated effusion is highly suggestive of empyema.

Treatment:

1. Uncomplicated parapneumonic effusion: Antibiotic.
2. Complicated parapneumonic effusion: Thoracotomy tube should be inserted in the following situations:
 - Gross pus.
 - Gram staining of fluid shows positive organism.
 - Glucose is <50 mg/dL.
 - $\text{pH} < 7.00$.
3. If pleural fluid is loculated and not adequately drained: streptokinase injection 250,000. Or, urokinase 100,000 units should be injected intrapleurally to dissolve fibrin membrane.
4. If still inadequate drainage: thoracoscopy with breakdown of adhesion or thoracotomy with decortication should be done.

Q: How can you suspect malignant effusion?

A: As follows:

- Elderly emaciated patient.
- Presence of generalized clubbing and nicotine stain.
- Palpable lymph node.
- Radiation mark in chest.
- Pleural fluid is haemorrhagic.
- There is rapid accumulation after aspiration.

Q: What are the differences between traumatic haemothorax and haemorrhagic pleural effusion?

A: As follows:

	Traumatic Haemothorax	Haemorrhagic Pleural Effusion
1.	Less uniform	Uniformly mixed
2.	Usually clots on standing	Does not clot
3.	Gross haemorrhage, $\text{RBC} > 100,000/\text{mm}^3$	$\text{RBC} > 10,000/\text{mm}^3$
4.	RBC not crenated (fresh RBC)	RBC may be crenated

Q: What are the causes of haemothorax?**A:** As follows:

- Chest injury or trauma.
- Bronchial carcinoma.
- Pleural mesothelioma.
- Pulmonary infarction.
- Others: SLE, lymphoma, acute pancreatitis.

Q: What is empyema? What are the causes?**A:** Accumulation of pus in the pleural cavity is called empyema. Causes are:

1. Tubercular.
2. Non-tubercular:
 - Bacterial pneumonia.
 - Lung abscess (bursting in pleural cavity).
 - Bronchiectasis.
 - Secondary infection after aspiration.
 - Rupture of subphrenic abscess or liver abscess.
 - Infected haemothorax.

Q: How to diagnose empyema thoracis clinically?**A:** As follows:

1. **Symptoms:**
 - High fever, sometimes hectic, associated with chill, rigor and sweating. Fever is persistent even with antibiotic.
 - Malaise, weight loss.
 - Copious purulent sputum if empyema ruptures into a bronchus (bronchopleural fistula).
2. **Signs:**
 - Patient is toxic, emaciated.
 - Tachypnoea, tachycardia.
 - Clubbing.
 - To be confirmed: Aspiration that shows pus or purulent fluid.

Q: How to treat empyema thoracis?**A:** According to cause:

1. Non-tuberculous:
 - Drainage of pus.
 - Antibiotic for 2 to 6 weeks. I/V co-amoxiclav or cefuroxime plus metronidazole. Antibiotic may be needed according to C/S.
 - If the pus is thick or loculated: surgical intervention may be needed.
2. Tuberculous empyema:
 - Wide bore needle aspiration or intercostal tube drainage.
 - Antitubercular therapy.
 - Sometimes surgical ablation of pleura.

Q: What is empyema necessitans?**A:** In empyema thoracis, fluid may come out subcutaneously in the chest wall. This is called empyema necessitans.

Q: What are the **causes** of bilateral effusion?

A: As follows:

- All causes of transudative effusion (CCF, nephrotic syndrome, cirrhosis of liver, malabsorption, malnutrition or hypoproteinaemia).
- Collagen disease (rheumatoid arthritis, SLE).
- Lymphoma.
- Bilateral extensive pulmonary TB.
- Pulmonary infarction.
- Malignancy (usually multiple metastases involving both lungs).

Q: What is **subpulmonary** pleural effusion?

A: Effusion between the lower surface of lung and upper surface of diaphragm. Confused with subphrenic abscess. Detected by chest X-ray in lateral decubitus position, or USG or CT scan.

Q: What is the **mechanism** of tuberculous pleural effusion?

A: Hypersensitivity to tuberculous protein in pleural space.

Q: What are the **causes** of recurrent pleural effusion? What is the **treatment**?

A: As follows:

- Bronchial carcinoma (commonest cause).
- Pleural mesothelioma.
- Lymphoma.
- Collagen disease (SLE).
- All causes of transudate.

Treatment of recurrent effusion: By pleurodesis.

Q: How **pleurodesis** is done?

A: In the following way:

- A plain rubber tube is introduced in the intercostal space and fluid is removed as far as possible. Administer the drug, tetracycline (500 mg) or kaolin or talc through the tube, clamp it and keep for 4 to 8 hours (may be overnight). In malignant pleural effusion, bleomycin 30 to 60 mg is introduced.
- Patient's posture should be changed 2 hourly to allow the drug to spread in pleural space.
- After 4 to 8 hours, remove any remaining fluid and take out the drainage tube at the height of inspiration.
- The patient usually complains of severe chest pain after pleurodesis. In such case, analgesic should be given.

Q: How to **differentiate** between chylothorax and empyema?

A: In both cases, fluid may be cloudy. It is centrifuged and following findings are observed:

- If clear—empyema.
- If persistently cloudy or milky—chylothorax.

Q: What is chylothorax? What are the causes?

A: It is the milky or whitish fluid in the pleural cavity due to lymphatic injury or obstruction of thoracic duct. Causes are:

- Traumatic (surgery and trauma to the thoracic duct).
- Neoplastic (bronchial carcinoma and metastasis).
- Infective (TB and filariasis).
- Lymphoma involving thoracic duct.

Q: What are the mechanisms of pleural effusion?

A: Excess pleural fluid accumulation occurs when pleural fluid formation exceeds absorption or normal pleural fluid formation with reduced absorption. Probable mechanisms are:

- Increased hydrostatic pressure (as in CCF).
- Reduced plasma colloidal osmotic pressure (as in hypoproteinaemia).
- Involvement of pleura causing increased permeability (as in TB and tumour).
- Impaired lymphatic drainage of pleural space (as in obstruction of lymphatic system by tumour, TB and radiation).
- Transdiaphragmatic passage of fluid (in liver disease, ascites and acute pancreatitis).

Features of rheumatoid pleural effusion:

1. Common in male, occurs in 3% cases of RA.
2. Usually small effusion, more in left side (cause unknown), may be bilateral.
3. Pleural fluid is serous in early case, later turbid, never blood stained (unless trauma).
4. Rheumatoid factor is usually positive, nodules usually present in the lung, systemic features are more.
5. Pleural fluid study:
 - Exudative (high protein, glucose is low).
 - High cholesterol (fluid looks turbid), with high LDH, low C₃ and C₄.
 - Rheumatoid factor in pleural fluid may be positive.
 - In the fluid: elongated macrophage, giant multi-nucleated macrophage and few mesothelial cells may be present.

Characteristics of tuberculous pleural effusion:

- Straw or amber colour.
- Exudative.
- High lymphocyte in pleural fluid.
- AFB is found in 20% cases.
- Culture for AFB is found in 1/3rd cases.
- Pleural biopsy is positive in 80% cases.

Q: What are the indications of pleural fluid aspiration?

A: Diagnostic and therapeutic:

1. Diagnostic: To see the physical character, cytology (polymorph and lymphocytes), exfoliative cytology (malignant cell), biochemistry (protein and sugar), ADA.
2. Therapeutic: Respiratory distress, massive effusion.

Q: How to treat pleural effusion?**A:** Treatment is given according to cause:

- Aspiration of fluid.
- If tuberculosis: Antitubercular therapy. Prednisolone 20 to 30 mg daily for 4 to 6 weeks, especially in large effusion.
- If parapneumonic: Aspiration of fluid, repeated if necessary. Antibiotic should be given. In complicated case, especially empyema, thoracostomy may be done. If all fails, thoracotomy with decortication may be necessary.
- If malignancy: Treatment is given accordingly. Because of recurrent effusion, pleurodesis is necessary.
- Treatment of primary disease: CLD, CCF, Nephrotic syndrome etc. should be given.

Q: How much fluid may be drawn at a time?**A:** Usually up to 1500 ml. If more is drawn, there is risk of re-expansion pulmonary oedema.

The mechanism is: due to effusion, lung is compressed and there is ischaemia to lung parenchyma and necrosis of pulmonary vessels. If more fluid is drawn, rapid expansion of the lung occurs. As necrotic vessels have not regenerated yet, there is more leakage of fluid which causes pulmonary oedema.

Q: What is the role of steroid in pleural effusion?**A:** Steroid is usually given in tubercular pleural effusion. Although its role is controversial, some evidence suggests that it promotes rapid absorption of pleural fluid and gives the patient quick symptomatic relief. It also prevents pleural fibrosis, thickened pleura and adhesion. Steroid should be used along with antitubercular therapy.**Q: What is the problem with steroid therapy in tuberculous pleural effusion?****A:** Steroid induces synthesis of hepatic enzymes, which causes breakdown of rifampicin. So the doses of rifampicin may need to be increased.

PNEUMOTHORAX

Instruction by the examiner:

- Examine the chest for respiratory system.
- Percuss and auscultate the front of the chest.

Presentation of a Case (Supposing Right Sided, Tell the Findings in Right Side):

On inspection:

- Restricted movement.
- Intercostal spaces: may appear full.

On palpation:

- Trachea and apex beat: shifted to the left.
- Vocal fremitus: reduced in right side, but normal in left side.
- Chest expansion: reduced on the right side.

On percussion:

- Hyperresonance in right side (mention up to where), but normal in left side.

On auscultation:

- Breath sound: diminished or absent in right side (mention up to where), but vesicular in left side.
- Vocal resonance: diminished or absent in right side (mention up to where), but normal in left side.

My diagnosis is **Right sided pneumothorax**.

Q: What are your **differential** diagnoses?

A: Giant bullae and big pulmonary cavity.

Q: What are the **definitive signs** of pneumothorax?

A: Hyperresonance on percussion and diminished or absent breath sound on the affected side.

Q: What is **pneumothorax**?

A: Pneumothorax means presence of air in the pleural cavity.

Q: What is the **usual presentation** of pneumothorax?

A: The patient usually presents with sudden onset of unilateral pleuritic chest pain, breathlessness.

Q: Mention **one** investigation for your diagnosis.

A: X-ray chest P/A view.

Q: What **investigations** do you suggest?

A: As follows:

- CBC with ESR.
- Chest X-ray P/A view.
- Sometimes, CT scan of chest.
- Other investigations according to suspicion of cause.

Q: What are the **types** of pneumothorax?

A: As follows:

1. Spontaneous: It may be primary and secondary.
2. Traumatic.

Q: What are the **causes** of pneumothorax?

A: As follows:

1. Spontaneous:
 - a. Primary: No evidence of underlying lung disease. However, some causes are:
 - Rupture of apical subpleural bleb due to congenital defect in connective tissue of alveolar walls. Common in young, 15 to 30 years of age. M:F ratio is 6:1. Patient is tall, lean and thin, 25% chance of recurrence.
 - Rupture of emphysematous bullae or pulmonary end of pleural adhesion.
 - b. Secondary: Due to pre-existing lung disease. Causes are:
 - Commonly COPD and tuberculosis.
 - Others: Lung abscess, acute severe asthma, bronchial carcinoma, pulmonary infarction, fibrotic and cystic lung disease, Marfan's syndrome, Ehlers–Danlos syndrome and eosinophilic granuloma.
2. Traumatic:
 - a. Iatrogenic: aspiration of pleural fluid, thoracic surgery, lung biopsy or pleural biopsy, positive pressure ventilation, thoracocentesis and subclavian vein catheterization.
 - b. Chest wall injury.

N.B.: Remember the following points:

- In young patient, common cause is rupture of subpleural bleb.
- In patient >40 years of age, common cause is COPD.

READ THE FOLLOWING TOPICS IN RELATION TO PNEUMOTHORAX

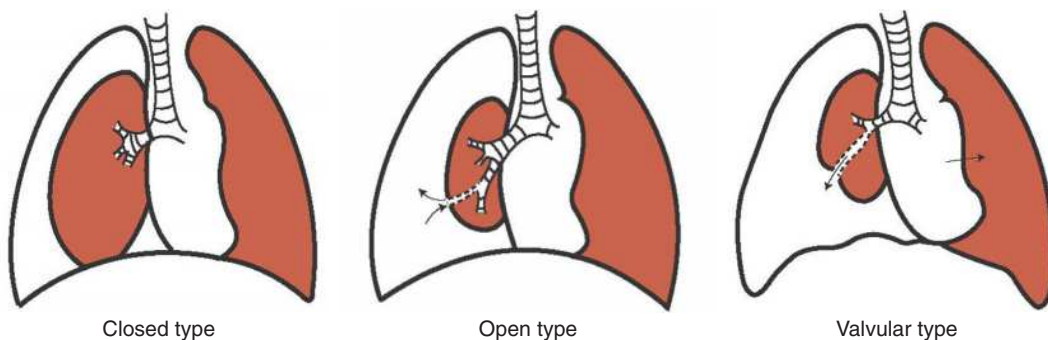
Q: What are the **types** of spontaneous pneumothorax?

A: 3 types (anatomical):

1. Closed: Communication between the lung and pleural space is sealed off. Intrapleural pressure < atmospheric pressure. Trapped air is slowly reabsorbed, lung re-expands in 2 to 4 weeks. Closed pneumothorax may be mild, moderate and large.
2. Open: Communication between the lung and pleural space persists (bronchopleural fistula). Intrapleural pressure and atmospheric pressure are equal throughout the respiratory cycle, which prevents re-expansion of the collapsed lung. Hydropneumothorax develops. Infection is common and empyema develops. Physical examination shows features of hydropneumothorax. Causes are:
 - Rupture of emphysematous bullae.
 - Small pleural bleb.
 - Tuberculous cavity.
 - Lung abscess into pleural cavity.

3. **Valvular:** There is a communication between the pleura and the lung, which acts as one way valve. Air enters into the pleural space during inspiration, but does not come out during expiration. Intrapleural pressure becomes greater than the atmospheric pressure. It results in compression of the lung, shifting of mediastinum to the opposite side, compression of heart and the opposite lung also. It reduces the venous return by compressing SVC.

There is rapidly progressing breathlessness, cyanosis, shock etc. It is called tension pneumothorax, a medical emergency, death may occur within minutes.



N.B.: Normal intrapleural pressure is negative (subatmospheric), usually -2.5 to -6.0 mmHg.

Q: How would you grade pneumothorax?

A: According to British Thoracic Society:

- Mild: Small rim of air around the lung, $<20\%$ of the radiographic volume.
- Moderate: Lung collapse, >20 to 50% of the radiographic volume.
- Large: Lung collapse, $>50\%$ of the radiographic volume.
- Tension: Pneumothorax with cardiorespiratory distress and features of shock.

Above classification of the size of a pneumothorax tends to underestimate its volume. Latest classification by BTS is as follows. In these new guidelines, the size of a pneumothorax is divided into:

- 'Small' or 'large' depending on the presence of visible rim, 2 cm or >2 cm between the lung margin and the chest wall.
- 'Small' pneumothorax is <2 cm and 'large' pneumothorax is >2 cm.

Q: What **relevants** would you like to see to find out the causes?

A: As follows:

- Features of COPD.
- Signs of previous intercostal drain scar.
- Recent pleural aspiration/biopsy mark.
- Recent pacemaker insertion.
- Recent central venous access.
- Raised JVP (hallmark of tension pneumothorax).

Q: What is the **role of CT scan** to diagnose pneumothorax?

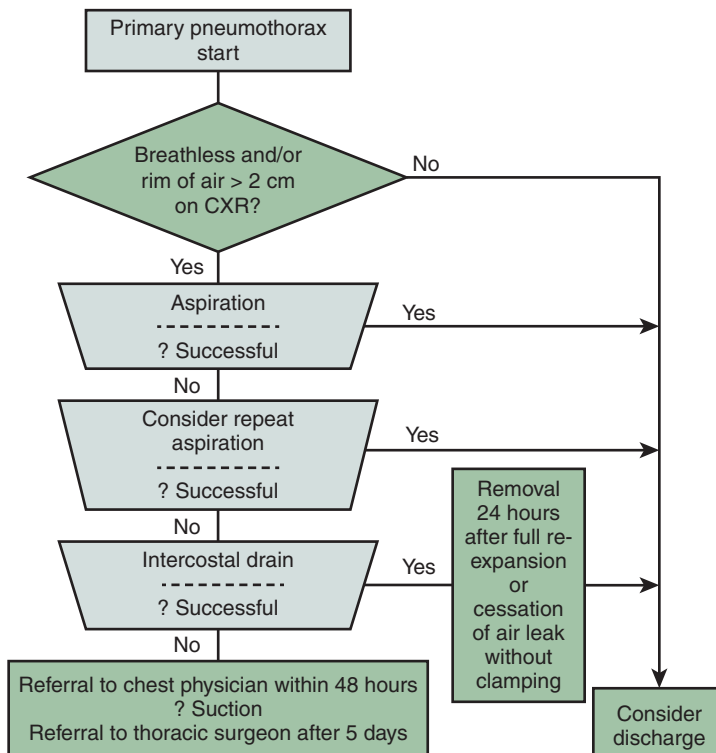
A: CT scan should be done to differentiate pneumothorax from complex bulla or when chest x ray is obscured by surgical emphysema.

Q: How to treat pneumothorax?

A: Depends on whether it is primary or secondary, open, closed or tension or presence of symptoms.

1. In primary pneumothorax:

- In small (<2 cm) closed pneumothorax without significant breathlessness: observation of case. The patient may be discharged with early outpatient review. Advice is given to return, if the patient develops breathlessness.
- Other treatment options: see the following chart (according to BTS guidelines):



2. In secondary pneumothorax:

- All patients should be hospitalized for observation.
- In small (<1 cm) or isolated apical pneumothorax in asymptomatic patient, observation of the patient.
- If age <50 years, asymptomatic or small pneumothorax, simple aspiration. If successful, 24 hours observation prior to discharge. If unsuccessful, intercostal drain tube should be inserted.
- If age >50 years, symptomatic or large pneumothorax, intercostal drain tube should be inserted.

3. Open pneumothorax: Surgery (as is due to bronchopleural fistula).
4. Tension pneumothorax (see below).

Advise to the patient:

- Must stop smoking.
- Avoid air travel for 6 weeks after normal chest X-ray.
- Diving should be permanently avoided.

Q: What are the causes of recurrent pneumothorax (more than twice)? How to treat?

A: Causes are:

- Apical subpleural bleb or cyst (congenital).
- Emphysematous bullae.
- Cystic fibrosis.
- Others: Marfan's syndrome, catamenial pneumothorax, Ehlers–Danlos syndrome, α_1 -antitrypsin deficiency, histiocytosis X (now named as Langerhans cell histiocytosis), honey comb lung.

Treatment:

1. Chemical pleurodesis—Done by injecting tetracycline (500 mg), kaolin or talc into pleural cavity through intercostal tube.
2. Surgical pleurodesis—Done by parietal pleurectomy or pleural abrasion during thoracotomy or thoracoscopy. Indications are:
 - All patients after second episode of pneumothorax.
 - Considered after first episode of secondary pneumothorax, if there is low respiratory reserve.
 - Patient who plan to continue activity, where pneumothorax would be particularly dangerous (e.g., flying or diving) should undergo definitive treatment after first episode of primary spontaneous pneumothorax.

N.B.: Pleurodesis is avoided in patient with cystic fibrosis, as lung transplantation may be required and pleurodesis may make this condition technically not feasible.

Q: What are the indications of surgery (open thoracotomy)?

A: As follows:

- Failure of the lung to re-expand after 5 days of tube thoracotomy.
- Recurrence (usually on third recurrence).
- Bilateral spontaneous pneumothorax.
- Professions at risk (e.g., pilots, divers).

Q: What is catamenial pneumothorax?

A: If pneumothorax develops at the time of menstruation, it is called catamenial pneumothorax. It is usually on the right side, occurs within 48 h of onset of menstruation, common in 25 to 30 year old female and is due to intrapleural endometriosis. Most catamenial pneumothoraces are small and self resolving. In some cases, it is treated by hormone therapy to suppress ovulation (by progesterone or androgen therapy) or simply by oral contraceptive pills. Sometimes, surgical exploration and pleurodesis may be needed.

Q: What is tension pneumothorax? What are the causes? How to treat?

A: It is a valvular type pneumothorax in which there is a communication between lung and pleural cavity with one way valve, which allows air to enter during inspiration and prevents to leave during expiration. It causes shifting of mediastinum to the opposite side, compresses opposite lung and heart (pressure in pleural space is positive and rises above atmospheric level).

Features are:

- Severe chest pain (pain is worse with cough and relieves on sitting position).
- Severe and progressively increasing dyspnoea.
- Tachypnoea, tachycardia, pulsus paradoxus.
- Features of shock (hypotension, central cyanosis and tachycardia).
- Raised JVP, engorged neck vein due to compression of the heart.
- Shifting of mediastinum.

N.B.: Cardinal features are progressively increasing dyspnoea and features of shock.

Causes of tension pneumothorax:

- Traumatic.
- Mechanical ventilation at high pressure.
- Rarely, spontaneous pneumothorax.

Treatment:

- High flow oxygen inhalation.
- Immediate insertion of wide bore needle in second intercostal space in mid-clavicular line, with the patient in sitting position.
- Intrathoracic tube is inserted in fourth, fifth or sixth intercostal space in mid-axillary line and the tip of the tube should be advanced in apical direction. It is connected to an underwater seal or one-way Heimlich valve.
- Patient should be kept propped up.
- Morphine 5 to 10 mg subcutaneously.
- If bubbling ceases, repeat chest X-ray. If the lung re-expands, tube may be removed after 24 hours. Tube should be removed during expiration or Valsalva manoeuvre (the tube need not be clamped before removing).
- If no response or continued bubbling for 5 to 7 days, surgical treatment may be necessary.

Q:How do you know that the **water seal drainage** is working properly or not?

A: As follows:

- Bubbling of air in water.
- During expiration or coughing, more bubbling occurs.
- During inspiration, water column ascends within the tube.

Q:What **advice** is given to the patient with water seal drainage?

A: As follows:

- Never raise the bottle above the chest wall. It must be kept below the level of thorax.
- The patient is also advised to inflate balloons or respirometer, which will help to expand the lung.

Q:How to **follow up** a patient after chest tube insertion?

A: Following findings should be seen:

- Bubbling: Whether it disappears or persists (indicates leaking).
- Blockage of the tube by clot or kinking.
- Malposition.
- Retrograde flow back into the chest.

Q: If you are working at a **remote place** and a patient presents with **tension pneumothorax**, what measures should you take?

A: Immediately I shall insert a wide bore needle (may be cannula/venflon) in the second intercostal space in mid-clavicular line. This will allow the trapped air to escape (producing an audible hiss). Then I shall send the patient to the nearest hospital (cannula should not be removed, must be taped tightly).

Q: How **long** the lung takes to re-expand?

A: Air is absorbed at the rate of 1.25% of the total radiographical volume in 24 hours. Hence, if there is 50% lung collapse, it will take 40 days to expand.

Q: What are the possible causes of **failure of re-expansion** of lung?

A: As follows:

- Water seal drainage is not working properly or may be blocked.
- Presence of bronchopleural fistula.
- A major bronchus may be obstructed.
- Lung is completely fibrosed with permanent damage.

Q: What is **hydropneumothorax**? What are the **causes**?

A: When there is accumulation of fluid and air in pleural cavity, it is called hydropneumothorax. Its causes are:

- Iatrogenic (during aspiration of pleural fluid).
- Pulmonary TB.
- Bronchopleural fistula.
- Trauma (penetrating chest injury and thoracic surgery).
- Rupture of lung abscess.
- Oesophageal rupture.
- Erosion of bronchial carcinoma.

Q: What is the **bedside test** in hydropneumothorax?

A: Succussion splash.

Q: What are the **signs** of hydropneumothorax?

A: In the lower part of chest, signs of pleural effusion and in upper part, signs of pneumothorax.

Q: What is the **treatment** of hydropneumothorax?

A: Water seal drainage and treatment of primary cause.

Q: What are the **indications** of chest tube or IT tube drainage?

A: As follows:

- Tension pneumothorax.
- Large second spontaneous pneumothorax if >50 years of age.
- Malignant pleural effusion.
- Empyema thoracis or complicated parapneumonic effusion.
- Hydropneumothorax.
- Traumatic haemopneumothorax.
- Postoperatively, e.g., thoracotomy, oesophagectomy, cardiothoracic surgery.

BRONCHIECTASIS

Instruction by the examiner:

- Examine the back of the chest.
- Or, auscultate the back of the chest.

Presentation of a Case:

- Breath sound is normal vesicular.
- Vocal resonance is normal in all the areas.
- Multiple coarse crepitations in right or left or both lung bases, or throughout the lung fields, altered by cough (mention accordingly).

My diagnosis is **Bronchiectasis** (right or left or bilateral or extensive).

Q: What **else** do you want to examine?

A: I want to examine for clubbing.

Q: What are your **differential diagnosis**?

A: As follows:

If unilateral:

- Resolution stage of pneumonia.
- Lung abscess.

If bilateral:

- Diffuse parenchymal lung disease (DPLD), or ILD.
- Chronic pulmonary oedema.

Q: Why it is bronchiectasis?

A: Because-

- Generalized clubbing involving both fingers and toes.
- On auscultation, basal coarse crepitations altered by coughing (mention whether unilateral, bilateral or both).

All are highly suggestive of bronchiectasis.

Q: What **history** do you like to take in bronchiectasis?

A: History of cough with profuse expectoration of sputum, which is more marked in the morning after waking up from sleep.

Q: Why not DPLD (or ILD)?

A: In DPLD (or ILD), crepitations are usually bilateral basal, inspiratory (dry or 'Velcro' type in quality), unaltered by coughing. In such case, there is history of persistent cough that may or may not be with profuse expectoration, progressively increasing breathlessness or exertional dyspnoea.

Q: Why not pulmonary oedema?

A: In pulmonary oedema—no generalized clubbing, crepitations are usually fine, present both in inspiration and expiration. Also, there is history of orthopnoea or paroxysmal nocturnal dyspnoea or history suggestive of any cardiac disease, HTN etc.

Q: What are the causes of basal crepitations?

A: As follows:

1. Unilateral basal crepitation:

- Unilateral bronchiectasis.
- Resolution stage of pneumonia.
- Lung abscess.
- Localized fibrosis of lung.

2. Bilateral basal crepitation:

- Bilateral bronchiectasis.
- DPLD (ILD or Fibrosing alveolitis).
- Pulmonary oedema.

3. Causes of bilateral crepitation with clubbing:

- Bilateral bronchiectasis.
- DPLD (ILD or Fibrosing alveolitis).

Q: What is the commonest site of bronchiectasis?

A: Left lower lobe and lingula.

Q: What is post-tussive crepitation? What is its significance?

A: Crepitation that appears after cough is called post-tussive crepitation. It is usually at the apex and indicates TB.

Q: What are the presentations of bronchiectasis?

A: Cough with profuse expectoration of sputum, more marked in the morning after waking from sleep. Occasionally, haemoptysis and breathlessness in advance cases. Features of secondary infection may be present.

Q: What is dry bronchiectasis (bronchiectasis sicca)?

A: It is a type of bronchiectasis in which dry cough is associated with intermittent episodes of haemoptysis. It may be massive, even life threatening. Bleeding occurs from bronchial vessels. Common in patient with granulomatous infection such as TB, usually involves upper lobe.

Q: Why haemoptysis?

A: It is due to bronchial wall hypertrophy, so mucosa becomes friable, sloughs out, capillary opens and bleeding occurs. Erosion of hypertrophic bronchial artery may result in massive haemoptysis.

READ THE FOLLOWING TOPICS IN RELATION TO BRONCHIECTASIS

Q: What is **bronchiectasis** and what are the **causes**?

A: It is the abnormal, permanent dilatation of one or more bronchi with destruction of bronchial wall proximal to the terminal bronchiole. Causes are:

1. Congenital or hereditary:
 - Cystic fibrosis.
 - Kartagener's syndrome (triad of bronchiectasis, dextrocardia and sinusitis or frontal sinus agenesis).
 - Primary ciliary dyskinesia (including immotile ciliary syndrome).
 - Hypogammaglobulinaemia (IgA and IgG which causes recurrent infection and bronchiectasis).
 - Yellow nail syndrome.
 - Young syndrome (obstructive azoospermia and chronic sinopulmonary infection, due to mercury intoxication).
 - Sequester segment of lung.
2. Acquired:
 - In children—pneumonia complicating measles, whooping cough, primary TB and foreign body.
 - In adults—pulmonary TB, recurrent aspiration or suppurative pneumonia, bronchial neoplasm.
 - Allergic bronchopulmonary aspergillosis (causes proximal bronchiectasis).

N.B.: Remember, the commonest causes of bronchiectasis are:

- *In children: post-measles or whooping cough.*
- *In adults: post-tubercular bronchiectasis are.*

Q: What are the **types** of bronchiectasis?

A: 3 types:

- Saccular or cystic (more severe form).
- Cylindrical.
- Fusiform.

Q: What are the **characteristics of sputum** in bronchiectasis?

A: If the sputum is kept in a bottle, 3 layers are observed:

- Lower sediment (epithelial debris and bacteria) layer.
- Middle thick or liquid layer.
- Upper frothy layer.

Q: What are the **complications** of bronchiectasis?

A: As follows:

- Secondary infection, common organisms are *Staph. aureus*, *H. influenzae* and *Pseudomonas aeruginosa*.
- Lung abscess.
- Massive haemoptysis.
- Pleural effusion, empyema or pneumothorax.
- Pulmonary hypertension and cor pulmonale.
- Respiratory failure.
- Amyloidosis (commonly involves spleen or kidney) in longstanding case.
- Brain abscess (metastatic cerebral abscess).
- Aspergiloma in the bronchiectatic cavity.

Q: If a patient with bronchiectasis develops **nephrotic syndrome** (or urine shows proteinuria), what is the likely diagnosis?

A: Amyloidosis (there may be splenomegaly).

Q: What **investigations** should be done in bronchiectasis?

A: As follows:

1. Chest X-ray PA view (may be normal). There may be:
 - Ring with clear centre (like honey-comb).
 - Ring with or without fluid level, may be multiple (cystic bronchiectasis).
 - Linear streaks (tram line).
 - Thick bronchi, signet ring or patchy opacity.
2. High resolution CT (HRCT): Definitive (preferred investigation).
3. Others:
 - CBC, ESR (may be neutrophilic leucocytosis).
 - X-ray of PNS (in Kartagener's syndrome).
 - Lung function tests (obstructive type usually, may be restrictive in advanced case).
 - Sputum for Gram staining, C/S, AFB, malignant cell (mention if necessary).
 - Sometimes bronchoscopy to locate the site of obstruction.
 - Aspergillus precipitin antibody or skin prick test (if **allergic bronchopulmonary aspergillosis** is suspected).
 - Serum immunoglobulin: In hypogammaglobulinaemia (10% adults with bronchiectasis have antibody deficiency, mainly IgA).
 - Sweat test for chloride content and cystic fibrosis genetic assessment: If cystic fibrosis is suspected.
 - Mucociliary clearance (nasal clearance of saccharin): Normally <30 min. If more, indicates ciliary dysfunction.
 - Nasal nitric oxide is a useful test for screening for primary ciliary dyskinesia (PCD). It is very low in PCD. Further ciliary investigation in a specialist centre may be required.
 - Urine for proteinuria (if amyloidosis is suspected).
 - USG of whole abdomen (if situs inversus is suspected).

Q: What is the **role of CT scan** in diagnosis of bronchiectasis?

A: Conventional CT has sensitivity of 60 to 80%, HRCT has sensitivity more than 90%.

Q: What is the **difference** between standard CT scan and HRCT?

A: In standard CT, resolution is 10 mm thick. But in HRCT, resolution is 1 to 2 mm thick.

Q: How will you **treat** bronchiectasis?

A: As follows:

1. Postural drainage, keeping the affected part remaining up, percuss over it, done for 5 to 10 min, once or twice daily.
2. Chest physiotherapy.
3. Daily airway clearance therapy.
 - Active cycle of breathing technique may be used. Devices to assist this, such as the 'Flutter' or 'Acapella' may be used, which provide positive expiratory pressure with or without airway oscillation.
 - Nebulized hypertonic saline is also helpful.

4. Antibiotic, if infection. *Pseudomonas aeruginosa* and *H influenzae* are common organisms.
 - For *Pseudomonas aeruginosa*, ciprofloxacin (750 mg twice daily).
 - *H influenzae*, amoxicillin, co-amoxiclav or doxycycline may be used.
 - In multi-resistant species, intravenous cephalosporin (e.g., Ceftriaxime) may be given.
5. Mucolytic such as N-acetylcysteine, bromhexine, erdosteine, carbocysteine.
6. Bronchodilator drugs: Nebulized salbutamol may be used as in bronchial asthma, COPD, cystic fibrosis and ABPA (Allergic Bronchopulmonary Aspergillosis).
7. Inhaled or oral steroid: decreases the rate of progression, helpful in ABPA.
8. Long-term azithromycin has an immunomodulatory effect. It reduces frequency of exacerbation.
9. Vaccination for influenza and pneumococcus should be given.
10. Surgery:
 - Lobectomy.
 - In bilateral extensive bronchiectasis: lung transplantation is required.

Indications of Surgery: Usually in Young Patient. Indications are-

- Unilateral and localized to a single lobe or segment.
- Severe and recurrent haemoptysis.

BRONCHIECTASIS WITH CYSTIC FIBROSIS

Instruction by the examiner:

- Examine the back of the chest. Or, auscultate the back of the chest.

Presentation of a Case:

- Present the case as written in bronchiectasis (Patient is young with features of bronchiectasis).

My diagnosis is **Bronchiectasis**.

Q: What do you think the **cause** is in this young patient?

A: I want to take the history. It may be pneumonia complicating measles or whooping cough in childhood. Also, it may be due to cystic fibrosis.

Q: Why cystic fibrosis?

A: Because the patient is young (or child) with bilateral extensive bronchiectasis involving both lungs with generalized clubbing.

Q: What is **cystic fibrosis**?

A: Cystic fibrosis is an autosomal recessive disease characterized by abnormal transport of chloride and sodium ions across the epithelium, causing thick and viscous secretions, leading to bronchopulmonary infection and pancreatic insufficiency. Incidence is 1 in 2500 live births, carrier rate is 1 in 25.

Q: What is the **pathogenesis** of CF?

A: CF is due to mutation of a gene on the long arm of chromosome 7, which codes for chloride channel known as cystic fibrosis transmembrane conductance regulator (CFTR), which regulates salt and water movement across the epithelium of nose, lungs, salivary glands, pancreas, intestine and bile ducts.

Q: What are the **clinical features** of cystic fibrosis?

A: Features depend on the age of the patient:

Neonate: Failure to thrive, meconium ileus, rectal prolapse.

Children and young adult:

1. Respiratory:

- Recurrent infection (by *Staph. aureus*, *Pseudomonas aeruginosa* are the commonest).
- Features of bronchiectasis: cough with profuse expectoration, wheeze, haemoptysis.
- May be pneumothorax, lung collapse, respiratory failure, cor pulmonale, asthma, otitis media, sinusitis, nasal polyps.

2. Abdominal:

- Pancreatic insufficiency causing steatorrhoea, malabsorption.
- Cholesterol gallstone.
- Secondary biliary cirrhosis and portal hypertension.
- Distal intestinal obstruction syndrome (meconium ileus equivalent syndrome).
- Increased incidence of peptic ulceration and GI malignancy.

3. Others:

- CF related diabetes, in 25% cases.
- Male infertility (due to failure of development of vas deferens and epididymis). About 20% of females with cystic fibrosis are infertile.
- Delayed puberty and skeletal maturity.
- Arthritis, osteoporosis.
- Cutaneous vasculitis.
- Clubbing with hypertrophic osteoarthropathy.
- Stress incontinence due to repeated forced cough.
- Low body mass index.

Q: What is **distal intestinal obstruction syndrome** (previously known as meconium ileus equivalent syndrome)?

A: It is a form of small intestinal obstruction in a patient with cystic fibrosis, due to combination of steatorrhoea and viscid intestinal secretions, causing recurrent abdominal pain, faecal impaction in ascending colon or ileocaecal junction, abdominal distention and flatulence. Present at any time after the neonatal period but more common in the 2nd and 3rd decades of life.

Q: How to **diagnose** cystic fibrosis?

A: As follows:

- In newborn—screening by measuring immunoreactive trypsinogen by heel prick test. If the concentration is raised, formal testing is performed.
- Family history of cystic fibrosis.
- Sweat test (pilocarpine iontophoresis): High sweat chloride concentration >60 mmol/L (normal range is <30 mmol/L).
- Blood DNA analysis of gene defect.
- Radiological features of bronchiectasis.
- Absent vas deferens and epididymis.
- Blood immunoreactive trypsin levels (for screening purpose).

Q: What **investigations** should be done in cystic fibrosis?

A: As follows:

1. Routine

- CBC.
- Blood sugar
- Liver function tests.
- Serum creatinine and electrolytes.
- Throat swab and sputum culture.
- X-ray chest (shows hyperinflation, bronchiectasis).
- USG of whole abdomen (fatty liver, cirrhosis, chronic pancreatitis).
- Spirometry (to see obstructive defect).
- Faecal fat analysis.

2. Specific

- Sweat test (high sweat chloride concentration >60 mmol/L).

Q: How to treat cystic fibrosis?**A:** As follows:

1. General measures:
 - Nutritional support.
 - Fat soluble vitamin supplement.
 - Strict glucose control.
 - Smoking must be stopped.
 - Vaccination for influenza and pneumococcus.
2. For respiratory problems:
 - Regular physiotherapy (postural drainage, active cycle techniques, forced expiratory techniques).
 - Symptomatic relief by mucolytic, inhaled bronchodilator (albuterol), inhaled corticosteroid.
 - Recombinant human DNase (rhDNase) is advised for routine treatment from early childhood (regardless of disease status).
 - Hypertonic saline, inhaled mannitol may give some relief.
 - Antibiotic for infection.
 - Prophylactic (oral ciprofloxacin or nebulized colistimethate, colomycin, aztreonam, levofloxacin or tobramycin). Azithromycin 500 mg orally 3 times a week, has immunomodulatory properties.
 - Oxygen therapy, as needed.
 - Pulmonary rehabilitation.
 - Ivacaftor is an oral drug, a potentiator of CFTR channel.
 - For advanced lung disease: Oxygen, diuretics (for cor pulmonale), non-invasive ventilation, lung or heart–lung transplantation.
3. For abdominal problems:
 - Pancreatic enzyme and vitamin supplementation.
 - If acute abdomen due to intestinal obstruction: Nothing by mouth, IV fluid and nasogastric suction should be given. Acetylcysteine given intravenously or through the nasogastric tube is useful in resolving bowel obstruction.
 - Ursodeoxycholic acid for impaired liver function.
 - Liver transplantation may be needed in cirrhosis.
4. Others: Treatment for osteoporosis, arthritis, sinusitis, vasculitis and infertility.
5. Gene therapy is a possibility in future.
6. Genetic counselling.

N.B.: Remember the following points:

- Cystic fibrosis should be suspected in any young patient with chronic respiratory and chronic gastrointestinal problem.
- Gastrointestinal problems, malabsorption and diabetes mellitus in cystic fibrosis is due to pancreatic insufficiency.
- Faecal elastase is used as a screening test for exocrine pancreatic dysfunction.
- Pseudomonas aeruginosa is the commonest organism, causing recurrent respiratory infection.
- Prognosis: Median survival is 36 years.
- Patient should be seen every 3 months and have an annual review. Lung function (FEV1) and BMI should be recorded at every appointment, as they have prognostic importance.

DPLD (PREVIOUSLY CALLED FIBROSING ALVEOLITIS OR ILD)

Instruction by the examiner:

- Examine the chest. Or, auscultate the back of the chest.

Presentation of a Case:

Inspection:

- The patient is dyspnoeic, hyperventilating with cyanosis (mention if present).
- Respiratory rate is 30/min.

Palpation:

- Trachea is central in position.
- Apical beat is in left fifth intercostal space, just medial to the midclavicular line.
- Chest expansion is reduced symmetrically.
- Vocal fremitus is normal.

Percussion:

- Percussion note is resonant over both lung fields.

Auscultation:

- Breath sound is vesicular with prolonged expiration.
- **Bilateral basal end inspiratory fine crepitations are present, which are unaltered by coughing.**
- Vocal resonance is normal.

My diagnosis is **DPLD (fibrosing alveolitis or ILD)**.

Q: What **relevants** do you like to see?

A: As follows:

- **Clubbing.**
- **Cyanosis (usually central).**
- Others to find out cause: **Features of rheumatoid arthritis, systemic sclerosis, dermatomyositis, SLE, history of drugs.**

***N.B.:** Triad of clubbing, cyanosis and bilateral end inspiratory fine crepitation is highly suggestive of DPLD.*

Q: What are your **differential diagnoses**?

A: As follows:

- **Bilateral bronchiectasis.**
- **Fibrosis of the lung due to other causes.**
- **Chronic heart failure (pulmonary oedema).**

Q: Why not pulmonary oedema?

A: In pulmonary oedema, crepitations are usually fine, present both in inspiration and expiration, altered by coughing. Clubbing is absent in pulmonary oedema. Also, in pulmonary oedema, there may be history of orthopnoea, PND or cardiac disease.

Q: Why is there **end-inspiratory crepitations** in DPLD?

A: In DPLD, alveoli remain collapsed. During forceful inspiration, sudden opening of collapsed alveoli produces crepitations.

Q: What are the causes of **bilateral crepitations**?

A: See in the topic 'bronchiectasis'.

Q: What are the causes of **clubbing with bilateral basal crepitations**?

A: See in the topic 'bronchiectasis'.

READ THE FOLLOWING TOPICS IN RELATION TO DPLD

Q: What is **DPLD**?

A: DPLD are a heterogeneous group of diseases characterized by diffuse lung injury and inflammation that can progress to lung fibrosis. Previously, it was called interstitial lung disease (ILD).

Q: Why is it called **DPLD**?

A: The term DPLD is preferred than ILD, because the pathological lesion involves the alveoli along with interstitium.

Q: What **history** do you like to take in **DPLD**?

A: As follows:

- Onset of the disease: Acute or chronic.
- History of connective tissue disease like rheumatoid arthritis, systemic sclerosis, dermatomyositis, SLE.
- History of drugs and smoking.
- Occupational and environmental history.

Q: What are the **presentations** of **DPLD (IPF)**?

A: Patient is usually elderly, uncommon <50 years.

- Cough, usually dry.
- Progressive breathlessness, usually exertional.
- Arthralgia, arthritis.
- Weakness, dizziness, giddiness.
- Cyanosis and finger clubbing (20 to 50% cases).

Q: **Classify DPLD.**

A: DPLD is classified into 6 groups:

1. Granulomatous DPLD (e.g., sarcoidosis).
2. Granulomatous DPLD with vasculitis (e.g., Wegener's granulomatosis, Churg–Strauss syndrome, microscopic vasculitis).
3. Idiopathic interstitial pneumonia (IIP):
 - a) Idiopathic pulmonary fibrosis (IPF), previously called cryptogenic fibrosing alveolitis (90%).
 - b) Idiopathic interstitial pneumonia other than IPF (10%):
 - Desquamated interstitial pneumonia.
 - Acute interstitial pneumonia.
 - Nonspecific interstitial pneumonia.
 - Respiratory bronchiolitis.
 - Cryptogenic organizing pneumonia (COP), also called bronchiolitis obliterans organizing pneumonia (BOOP).
 - Lymphocytic interstitial pneumonia.

4. Pulmonary autoimmune rheumatic diseases (e.g., rheumatoid arthritis, SLE).
5. Drugs (busulphan, bleomycin, methotrexate, nitrofurantoin, amiodarone).
6. Other forms of DPLD, e.g., histiocytosis X (Langerhans cell histiocytosis), Goodpasture syndrome, idiopathic pulmonary haemosiderosis, diffuse alveolar haemorrhage, lymphangioleiomyomatosis, pulmonary alveolar proteinosis.

Q: What investigations should be done in DPLD?

A: As follows:

1. CBC (shows different changes in different diseases):
 - ESR may be high (polycythaemia is rare).
 - Lymphopenia (in sarcoidosis).
 - Eosinophilia (in pulmonary eosinophilia and drug reactions).
 - Neutrophilia (in hypersensitivity pneumonitis).
2. X-ray chest shows:
 - Initially ground glass appearance, bilateral reticulonodular shadow mainly in lower zone. Lung size may be reduced, diaphragm may be raised.
 - In advanced stage, there may be honeycomb appearance.
3. HRCT: Helpful in early diagnosis, even when chest X-ray is normal.
4. Pulmonary function tests:
 - Restrictive pattern (FVC and FEV₁ are proportionately low and ratio is normal or high).
 - Lung volumes are reduced (may be paradoxically preserved in patient with concomitant emphysema).
 - Reduced carbon monoxide (CO) transfer.
 - Peak flow rate may be normal.
5. Arterial blood gas: Hypoxaemia with normal or low PaCO₂ (due to hyperventilation).
6. Bronchoscopy:
 - Bronchoalveolar lavage shows increased number of cells, particularly neutrophils and macrophages.
 - May be increased lymphocytes in sarcoidosis, extrinsic allergic alveolitis and drug-induced lung disease.
7. Others (according to suspicion of cause):
 - CRP may be high.
 - LDH (high indicates disease activity).
 - For sarcoidosis: Calcium is high. Urinary calcium excretion and liver biopsy may be useful. Serum ACE is an indicator of disease activity. Gallium scanning may be done.
 - For autoimmune diseases: such as, RA test and anti-CCP antibodies in rheumatoid arthritis, should be done. RA test and ANA are positive in 30% cases in DPLD (in low titre).
 - Hypergammaglobulinaemia.
8. For confirmation, lung biopsy is definitive, done in selected cases, if diagnosis is uncertain.

Q: How lung biopsy is done?

A: Biopsy is done in the following methods:

- Transbronchial biopsy.
- Video-assisted thoracoscopic (VATS) lung biopsy.
- Open lung biopsy in some cases.

N.B.: Remember the following points:

- Lung biopsy is not a routine investigation, done in selected cases.
- Typical clinical features and HRCT are sufficient for diagnosis.
- However, lung biopsy is strongly indicated in young patient.

Q: How to treat DPLD (IPF)?

A: As follows:

- Smoking must be stopped.
- Avoid air pollution (dust, fume).
- Control of infection with appropriate antibiotic.
- Treatment of primary disease, if any.
- Bronchodilator—salbutamol, terbutaline, ipratropium, tiotropium, oxitropium. Long-acting β agonist—salmeterol, formoterol.
- Oral theophylline (in some cases).
- Prednisolone 0.5 mg/kg with azathioprine 2 to 3 mg/kg. Prednisolone is given for 2 months then tapered to maintenance dose of 10 to 12.5 mg daily.
- Antifibrotic therapy—Pirfenidone, N-acetyl cysteine, Sildenafil, Bosentan, Etanercept.
- Single lung transplantation in young patient at advanced stage. Survival is 1 year in 60% cases.

Q: What is the prognosis of DPLD?

A: As follows:

- Usually 3 to 5 year survival in 50% cases.
- 65% in steroid responder.
- 25% in steroid non-responder.

Q: What are the complications of DPLD?

A: As follows:

- Pulmonary hypertension.
- Cor pulmonale.
- Respiratory failure.
- Chest infection.
- Bronchial carcinoma.

CONSOLIDATION

Instruction by the examiner:

- Examine the chest for respiratory system. Or, percuss and auscultate the chest.

Presentation of a Case (Supposing Right Sided, Mention All Findings in Right Side):

On inspection:

- Restricted movement.

On palpation:

- Trachea: Central and apex beat in normal position.
- Vocal fremitus is increased (mention the location . . .).

On percussion:

- Woody dullness (mention the location . . .).

On auscultation:

- Breath sound is bronchial (mention the location . . .).
- Vocal resonance is increased and there is whispering pectoriloquy (mention the location . . .).
- There is (mention, if any) few crepitations or pleural rub.

My diagnosis is **Right sided consolidation**.

Q: What are the differential diagnoses?

A: As follows:

- Lung abscess.
- Bronchiectasis.

Q: Why not it is lung abscess?

A: In lung abscess, there is high temperature and patient is toxic. Coarse crepitations on auscultation. There may be combined features of cavitation and consolidation. Clubbing may be present. In the history, profuse foul smelling sputum. X-ray will show cavity with air fluid level.

Q: Can it be tuberculosis?

A: In tuberculosis, usually there is no sign of consolidation. Moreover in the history, there will be low grade continued fever with evening rise, weight loss, anorexia, night sweat etc.

Q: Why not bronchiectasis?

A: In bronchiectasis, coarse crepitations, reduced or disappear on coughing. Clubbing may be present. In the history, there is profuse sputum production, more marked in the morning after waking from sleep.

Q: What is the typical character of sputum in consolidation?

A: The sputum is rusty.

Q: Is there any crepitation in consolidation? Why?

A: Crepitation may be present during resolution of pneumonia.

Q: What **investigations** should be done in consolidation?

A: As follows:

1. CBC, ESR:
 - In bacterial pneumonia: Polymorphonuclear leucocytosis.
 - In atypical pneumonia: Normal or slightly increased leucocytes.
 - In viral pneumonia: leucopenia.
2. X-ray chest: Shows homogenous opacity with air bronchogram (usually found after 12 to 18 hours). If associated with hilar lymphadenopathy, suggestive of *Mycoplasma pneumoniae*.
3. Sputum: Gram staining, C/S (aerobic and anaerobic).
4. Blood C/S (positive in pneumococcal pneumonia).
5. Arterial blood gas analysis.
6. Others (according to aetiology):
 - Pneumococcal antigen in serum.
 - For mycoplasma: anti mycoplasma antibody, Coomb's test, C/S in special media.
 - Antibody against virus, *Chlamydia*, *Legionella*.
 - Urinary *Legionella pneumophila* antigen.
 - CRP (high).

N.B.: Chest X-ray may reveal complications, such as pleural effusion. Also there may be cavitation (found in infection by Staphylococcus aureus and pneumococcal serotype 3).

READ THE FOLLOWING TOPICS IN RELATION TO CONSOLIDATION

Q: What is **consolidation**?

A: It means pneumonia, which is defined as 'inflammation in the lung parenchyma characterized by accumulation of secretion and inflammatory cells in the alveoli'.

Q: What are the **types** of pneumonia?

A: As follows:

1. **Anatomically of 2 types:**
 - Lobar: Commonly involves one or more lobe.
 - Lobular (bronchopneumonia): It is characterized by patchy alveolar opacity with bronchial and bronchiolar inflammation. Commonly involves both lower lobes.
2. **Clinically of 4 types:**
 - Community acquired pneumonia (CAP).
 - Nosocomial (hospital acquired).
 - Suppurative and aspiration pneumonia.
 - Pneumonia in immunocompromised.

Q: What are the **causes** of **community acquired pneumonia (CAP)**?

A: As follows:

- Typical organism: Streptococcus pneumoniae (50%), Klebsiella pneumoniae, Haemophilus influenzae, Staphylococcus aureus.
- Atypical organism: Mycoplasma pneumoniae, Legionella pneumophila, Chlamydia psittaci, Coxiella burnetii.
- Others: viral (influenza, parainfluenza, measles, respiratory syncytial virus in infancy, varicella, CMV), Actinomyses israelii.

Q: What are the pathological stages of CAP?**A:** 4 stages:

- Stage of congestion: Persists for 1 to 2 days.
- Stage of red hepatization (red and solid, like liver): Persists for 2 to 4 days.
- Stage of grey hepatization: Persists for 4 to 8 days.
- Stage of resolution: 8 to 9 days or more.

Q: What are the presentations of community acquired pneumonia (CAP)?**A:** The patient may present with:

1. Fever, may be with chill and rigor.
2. Cough, initially short, painful and dry. Later on, expectoration (during resolution), rusty sputum (due to *Streptococcus pneumoniae*).
3. May be dyspnoea, haemoptysis, pleuritic chest pain (may radiate to shoulder or abdomen).
4. Other features: anorexia, nausea and vomiting.
5. Extrapulmonary features:
 - Myalgia, arthralgia and malaise: common in *Legionella* and *Mycoplasma*.
 - Myocarditis and pericarditis: common in *Mycoplasma pneumoniae*.
 - Headache, meningoencephalitis and other neurological abnormalities: common in *Legionella pneumoniae*.
 - Abdominal pain, diarrhoea and vomiting, hepatitis: common in *Legionella pneumoniae*.
 - Labial herpes simplex reactivation: common in pneumococcal pneumonia.
 - Skin rashes, such as erythema multiforme and erythema nodosum: common in *Mycoplasma pneumoniae*.

Q: What are the risk factors of pneumonia?**A:** As follows:

- Age: <16 or >65 years.
- Co-morbidities: HIV infection, diabetes mellitus, chronic kidney disease, malnutrition.
- Upper respiratory tract infections, recent influenza infection or other viral respiratory infection.
- Pre-existing lung disease: such as cystic fibrosis, bronchiectasis, COPD, obstructing lesion (bronchial carcinoma, inhaled foreign body, inhalation from oesophageal obstruction).
- Lifestyle: cigarette smoking, excess alcohol, intravenous drug use.
- Iatrogenic: immunosuppressant therapy (prolonged use of steroid, cytotoxic drugs).
- Others: Hospitalized ill patient, indoor air pollution.

Q: What are the complications of pneumonia?**A:** As follows:

- Pulmonary: Lung abscess, pleurisy, pleural effusion, empyema thoracis, pneumothorax by *S. aureus*, fibrosis of lung, collapse, ARDS, delayed or slow resolution.
- Cardiovascular: Pericarditis, myocarditis, endocarditis, arrhythmia, peripheral circulatory failure.
- Neurological: Meningism, meningoencephalitis.
- Musculoskeletal: Septic arthritis.
- GIT: Meteorism (gaseous distension of stomach, intestine or abdomen).
- Others: Septicaemia, renal failure, hepatitis, ectopic abscess formation by *S. aureus*.

Q: What are the causes of slow or delayed resolution of pneumonia?

A: Delayed resolution means when the physical signs persist for more than 2 weeks and radiological features persist for more than 4 weeks after antibiotic therapy. Causes are:

- Incorrect microbiological diagnosis.
- Fungal, tubercular or atypical pneumonia.
- Improper antibiotic or insufficient dose.
- Bronchial obstruction (bronchial carcinoma, adenoma, foreign body).
- Empyema or atelectasis.
- Immunocompromised patient (HIV, diabetes mellitus, lymphoma, leukaemia, multiple myeloma).

Q: What are the causes of recurrent pneumonia (3 or more separate attacks)?

A: As follows:

- Bronchial obstruction (bronchial carcinoma, adenoma, foreign body).
- Lung disease (bronchiectasis, cystic fibrosis, sequester segment of lung, commonly left lower lobe).
- Aspiration (achalasia cardia, systemic sclerosis, pharyngeal pouch).
- Immunocompromised patient (HIV, DM, lymphoma, leukaemia, multiple myeloma).

N.B.: Remember the following points:

- CAP usually spreads by droplet infection and most cases occur in previously healthy individual.
- Physical signs of consolidation usually appear within 2 days, disappear within 2 weeks with proper treatment.
- Radiological opacity appears within 12 to 18 h and disappears within 4 weeks with proper treatment.
- If radiological opacity persists after 8 weeks (with treatment), it is called non-resolution.

Q: What are the criteria of assessment of severity of CAP?

A: CURB-65 criteria is used to assess the severity of CAP. Score 1 point for each of the following features:

- Confusion (mini mental score 8 or less or new disorientation in person, place or time).
- Urea >7 mmol/L or >20 mg/dl.
- Respiratory rate >30 /min.
- Blood pressure (systolic BP <90 mmHg and diastolic BP <60 mmHg).
- Age >65 years.

CURB-65 score is used for management of CAP:

- Score 0 or 1: Home treatment.
- Score 2: Hospitalization.
- Score 3 or more: Manage in hospital, may require ICU (especially if score is 4 or 5).

Other markers of severity of pneumonia:

- Chest X-ray: More than one lobe involved.
- $\text{PaO}_2 < 8$ kPa.
- Low albumin (<35 g/L).
- WBC (<4000 /cmm or $>20,000$ /cmm).
- Blood culture is positive.
- Other co-morbidities.
- Absence of fever in the elderly.

Q: What are the **indications** for referral for **ITU (intensive treatment unit) or ICU?**

A: As follows:

- CURB score 4 or 5.
- Persistent hypoxia despite high concentration of oxygen ($\text{PO}_2 < 8$ kPa or 60 mmHg).
- Progressive hypercapnoea.
- Severe acidosis.
- Shock.
- Depressed consciousness.

Q: How to **treat CAP?**

A: Sputum should be sent for C/S before starting antibiotic.

- General treatment: Rest, O_2 therapy, adequate hydration and chest physiotherapy.
 - Antibiotic (empirically with suspicion of cause):
1. Mild CAP:
 - Amoxicillin 500 mg 8 hourly orally or erythromycin 500 mg 6 hourly or clarithromycin 500 mg twice daily or azithromycin 500 mg daily.
 - If *S. aureus* is suspected: Clarithromycin 500 mg twice daily orally or IV, **plus** flucloxacillin 1 to 2 g 6 hourly IV.
 - If *Klebsiella* is suspected: Ciprofloxacin 200 mg IV 12 hourly, **plus** gentamycin 60 to 80 mg IV 8 hourly (see serum creatinine level) or gentamycin plus ceftazidime 1 g IV 8 hourly.
 - Duration of treatment: 7 to 10 days (up to 14 days).
 - If *Mycoplasma*, *Legionella* or atypical organism is suspected: Clarithromycin 500 mg twice daily orally or erythromycin 500 mg 6 hourly orally, or tetracycline or doxycycline may be used. Duration of treatment: 2 to 3 weeks.
 2. Severe CAP:
 - Clarithromycin 500 mg twice daily IV or erythromycin 500 mg 6 hourly IV.
 - **Plus** add one of the following-
 - a) Co-amoxiclav 1 to 2 g 8 hourly IV.
 - b) Cefuroxime 1.5 g 8 hourly IV.
 - c) Ceftriaxone 1 to 2 g IV daily.
 - d) Amoxicillin 1 g 6 hourly IV **plus** flucloxacillin 2 g 6 hourly IV.
 - e) If *S. aureus* is suspected: Flucloxacillin 2 g 6 hourly IV or sodium fusidate is added.

Q: What are the **criteria for discharge** of a patient with pneumonia from hospital?

A: To discharge, the patient should be clinically stable with no more than one of the following clinical signs:

- Temperature $> 37.8^\circ\text{C}$.
- Heart rate $> 100/\text{min}$.
- Respiratory rate $> 24/\text{min}$.
- Systolic BP < 90 mmHg.
- $\text{SaO}_2 < 90\%$.
- Inability to maintain oral intake.
- Abnormal mental status.

Q: What is nosocomial pneumonia? What are the causes and predisposing factors?

A: New episode of pneumonia occurring at least 2 days after admission in the hospital is called nosocomial pneumonia.

Causes are: If it occurs within 4 to 5 days of admission (early onset), organisms are similar to CAP. If it occurs later (late onset), common organisms are:

- Gram-negative Enterobacteriaceae (*Escherichia coli*, *Klebsiella* and *Pseudomonas aeruginosa*) are common.
- *S. aureus* including methicillin resistant *S. aureus* (MRSA).
- Anaerobic organism.

Predisposing factors for nosocomial pneumonia:

- Elderly patient.
- Bed bound, unconscious (e.g., CVD).
- Postoperative case (thoracic or abdominal surgery).
- Malignancy.
- Diabetes mellitus.
- Use of steroid, cytotoxic drugs, antibiotics.
- Prolonged anaesthesia, intubation, tracheostomy, IV cannula.
- Achalasia of cardia, dysphagia due to any cause, vomiting.
- Bulbar or vocal cord palsy.
- Nasogastric intubation.
- Abdominal sepsis, infected emboli.

Q: How to diagnose nosocomial pneumonia?

A: After admission in hospital, associated with the predisposing factors, if the patient develops cough with purulent sputum, fever associated with radiological infiltrate, leucocytosis or leucopenia, unexplained increase in oxygen requirement.

Q: How to treat nosocomial pneumonia?

A: Empirical antibiotic therapy should be started intravenously.:

1. In early-onset HAP:
 - If no antibiotic was given: co-amoxiclav or cefuroxime may be given.
 - If antibiotic was given: piperacillin/tazobactam or a third generation cephalosporin (e.g., cefotaxime) should be given.
2. In late onset HAP: antibiotic must cover Gram-negative organisms, *Staph. aureus* (including MRSA) and anaerobes:
 - A third generation cephalosporin (e.g., cefotaxime) with an aminoglycoside (gentamicin) *or*
 - A monocyclic β -lactam (e.g., aztreonam) and flucloxacillin.
 - If MRSA is suspected—IV vancomycin. If possible, oral doxycycline, rifampicin or linezolid may be given.
 - If pseudomonas infection is suspected—IV ciprofloxacin or ceftazidime or doripenem, carbapenem (meropenem) should be given.
 - Chest physiotherapy and oxygen, fluid and nutritional support should be given.

N.B.: Aspiration pneumonia is also common in hospital and involves multiple organisms with anaerobe. Treatment: IV Co-amoxiclav or cefuroxime plus metronidazole.

Q: What is bronchopneumonia?

A: It is defined as 'wide spread diffuse patchy alveolar opacity associated with bronchial and bronchiolar inflammation, often affecting both lower lobes'. In children, it occurs as a complication of measles or whooping cough and in elderly, as a complication following bronchitis or influenza.

Q: What is typical pneumonia?

A: Typical pneumonia is characterized by high temperature with cough, pleuritic chest pain, features of consolidation, caused by *S. pneumoniae*, *S. aureus* etc. Respiratory symptoms are more than constitutional symptoms.

Q: What is atypical pneumonia?

A: When pneumonia is caused by *Mycoplasma*, *Legionella*, *Coxiella*, *Chlamydia*. In these cases, constitutional symptoms are more than respiratory symptoms. Features are:

- Gradual onset.
- Dry cough.
- Low grade fever.
- Constitutional symptoms are more than respiratory symptoms (headache, myalgia, fatigue, nausea, vomiting).
- Less physical finding in the chest.

N.B: Remember the following points:

- *The term atypical pneumonia is abandoned as the clinical and radiological picture does not differ sufficiently from one organism to another.*
- *Mycoplasma pneumoniae is more common in young, rare in the elderly.*
- *Haemophilus influenzae is more common in the elderly, if underlying lung disease is present.*
- *Legionella pneumophila occurs in local outbreaks due to contaminated cooling towers in hotels, hospitals and other industrial buildings.*
- *Staphylococcus aureus is more common following an episode of influenza.*

Q: How to diagnose and treat Mycoplasma pneumoniae?

A: It is common in children and young adults, usually associated with headache, malaise, myalgia and severe cough. Physical signs are less marked. Epidemics occur in cycle every 3 to 4 years.

Investigations:

- WBC (normal).
- Chest X-ray (commonly lower lobe involvement), may show bilateral patchy consolidation.
- Cold agglutinin (positive in 50% cases).
- Antibody titre for *Mycoplasma pneumoniae*.
- Others (CFT and haemagglutination test).

Extrapulmonary complications of *M. pneumoniae*:

- Maculopapular skin rash, erythema multiforme and Stevens Johnson syndrome.
- Myocarditis and pericarditis.
- Haemolytic anaemia (Coombs test may be positive) and thrombocytopenia.
- Meningoencephalitis, Guillain-Barré syndrome and other neurological abnormalities.
- Myalgia and arthralgia.
- Hepatitis and gastrointestinal symptoms like vomiting, diarrhoea.

Treatment:

- Clarithromycin 500 mg twice daily orally or IV **or** erythromycin 500 mg 6 hourly orally or IV for 7 to 10 days.
- **Or**, doxycycline 100 mg twice daily.
- Rifampicin 600 mg 12 hourly.

Q: How to diagnose and treat *Legionella pneumophila*?

A: 3 patterns of Legionnaires' disease may occur:

- Outbreak of infection is usually associated with contaminated water supply or cooling system, or from stagnant water in cistern or shower head.
- Sporadic case, where source is unknown. It is usually common in middle-aged and elderly, more in smokers.
- Outbreaks may occur in immunocompromised patients, e.g., those on corticosteroid therapy. Diabetes and chronic kidney disease (CKD) also increase risk.

Features are:

- Initially viral-like illness with high fever, chill and rigor, malaise, myalgia and headache, dry cough, later productive and purulent.
- There may be nausea, vomiting, diarrhoea and abdominal pain.
- Mental confusion and other neurological signs, even coma may be present.
- Occasionally, renal failure and haematuria may be seen.

Investigations:

- WBC: Lymphopenia without marked leucocytosis.
- Chest X-ray: Shows lobar or multilobar shadowing. Small pleural effusion may be present. Cavitation is rare.
- Hyponatraemia.
- Hypoalbuminaemia.
- High ALT, AST, CPK.
- Direct immunofluorescent for *Legionella* in pleural fluid, sputum or bronchial washings.
- Culture on special media can be done, but takes 3 weeks.
- *Legionella* serology: fourfold rise is highly suggestive.
- Urine for antigen (highly specific).
- Urine R/E shows haematuria.

Treatment:

- Clarithromycin 500 mg twice daily orally or I/V or Erythromycin 500 mg 6 hourly orally or I/V for 7 to 10 days.
- Rifampicin 600 mg 12 hourly.

Prognosis: 10% mortality (may be up to 30% in elderly).

Q: What are the **differences** between bacterial and viral pneumonia?

A: As follows:

Points	Bacterial pneumonia	Viral pneumonia
1. Onset	Abrupt.	Less abrupt.
2. History of upper respiratory tract infection	Absent.	Present.
3. Systemic features	High-grade fever with chill and rigor.	Low-grade fever, headache and malaise, myalgia.
4. Cough	Initially dry, later rusty sputum or purulent.	Usually dry (extra-pulmonary features are more).
5. Pleuritic chest pain	Common.	Less common (respiratory complains are less common) and constitutional symptoms are more.
6. Physical signs of consolidation	Well marked.	Minimal.
7. Blood count	Leucocytosis.	Normal or leucopenia.
8. Chest X-ray	Lobar or segmental homogeneous opacity with air bronchogram.	Mottling or reticular pattern or patchy opacity or streaky.
9. Sputum culture	Organism found.	No organism.

COLLAPSE OF LUNG

Instruction by the examiner:

- Examine the chest for respiratory system.

Presentation of a Case: (Supposing Right Sided, Mention the Findings in Right Side):

On inspection:

- Restricted movement.
- Flattening of upper part of chest.
- Crowding of ribs.

On palpation:

- Trachea: Shifted to the right.
- Apex beat: Shifted to the right (mention the site).
- Vocal fremitus: Reduced or increased (mention accordingly).

On percussion:

- Dullness in upper part of chest (mention up to the site).
- Upper border of liver dullness is in the right fourth intercostal space in the midclavicular line.

On auscultation:

- Breath sound: Bronchial or diminished or absent (mention accordingly).
- Vocal resonance: Increased or decreased (mention accordingly).
- There is whispering pectoriloquy (present, if bronchial sound is present).

My diagnosis is **Right sided lung collapse**.

Q: What **relevants** do you like to see?

A: As follows:

- Clubbing with nicotine stain. Also, emaciated and radiation mark (indicates underlying cause is bronchial carcinoma).
- Palpable supraclavicular lymph node (indicates malignancy with metastasis, also may be lymphoma, TB).
- Thoracotomy scar (indicates pneumonectomy).
- History of bronchial asthma or COPD.

Q: What is your **differential diagnosis**?

A: As follows:

- Fibrosis.
- Pneumonectomy (in such case, thoracotomy scar is present).

Q: Why not this is a case of **pleural effusion**?

A: In pleural effusion, trachea and apex beat are shifted to the opposite side.

Q: Why not this is a case of **thickened pleura**?

A: In thickened pleura, there is no shifting of trachea and apex beat.

Q: Why not **consolidation**?

A: In consolidation, trachea and apex beat will not be shifted, percussion is woody dull.

Q: Could it be fibrosis?

A: It may be fibrosis. Signs of collapse and fibrosis are almost similar. However, some findings are highly suggestive of fibrosis, as it is a chronic process:

- Flattening of chest.
- Crowding of ribs.
- Drooping of the shoulder of the affected side.

These findings may be present in collapse also, if it is prolonged. All other signs of collapse are same as in fibrosis, but with less degree. To be confirmed, chest X-ray will help, which shows:

- In collapse, the X-ray shows homogeneous opacity. Evidence of bronchial obstruction (mass lesion) may be seen and diaphragm may be elevated.
- In fibrosis, non-homogeneous opacity, rib crowding and ring shadow due to dilatation of bronchi within the fibrosis may be seen.

N.B.: Signs of collapse depend on patency of the bronchus:

- *If bronchus is completely obstructed (central collapse): all the signs will be **collapsed** (absent or reduced).*
- *If bronchus is patent (peripheral collapse): there is bronchial sound and increased vocal resonance.*

Q: What are the types of collapse?

A: As follows:

A. Etiologically:

1. Compression collapse (passive): Due to pleural effusion, pneumothorax and hydropneumothorax. Trachea and apex beat are shifted to the opposite side.
2. Absorption collapse (active): Caused by bronchial obstruction due to any cause. Air is absorbed distal to the obstruction and affected part is collapsed. Causes are:
 - Neoplasm (bronchial carcinoma, adenoma).
 - Foreign body (inert object, artificial teeth).
 - Mucous plug (due to bronchial asthma, cystic fibrosis, post-operative).
 - Aspergilloma.
 - Pressure on bronchus from outside (enlarged lymph node, aortic aneurysm, pericardial effusion causing collapse of left lung and enlarged left atrium in mitral stenosis).
 - Rarely, congenital collapse due to absence of surfactant.

B. Anatomically:

1. Central: Mass lesion (shows more signs and symptoms).
2. Peripheral: Usually small collapse (shows less signs and symptoms).

Causes of collapse according to age:

- Neonate: Congenital due to low or absent surfactant, aspiration of meconium.
- Children: Foreign body.
- Young: Bronchial adenoma and foreign body.
- Elderly: Bronchial carcinoma and foreign body (artificial tooth).

Q: How can you **differentiate** central and peripheral collapse clinically?

A: As follows:

- In central collapse: Bronchus is completely obstructed. So, breath sound is diminished or absent. Vocal resonance is diminished or absent.
- In peripheral collapse: Bronchus is patent. So, breath sound is bronchial and vocal resonance is increased.

N.B.: Commonest cause of collapse:

- *Central: Bronchial carcinoma or adenoma, enlarged lymph node or foreign body.*
- *Peripheral: Mucus plugging, bronchial cast.*

Q: What **investigations** should be done in collapse of lung?

A: As follows:

- CBC.
- Chest X-ray, PA view (homogenous opacity, heart and lung shifted to the affected side), lateral view, if needed.
- CT scan of chest.
- Bronchoscopy (to see any obstruction, removal of foreign body, aspiration of any material, biopsy).

Q: What is **middle lobe syndrome**?

A: Middle lobe syndrome is the recurrent or persistent atelectasis of right middle lobe, which originates at acute angle and is completely surrounded by lymph nodes. It is frequently obstructed by enlarged lymph nodes due to malignancy or TB causing collapse of the lobe. There may be bronchiectatic changes. Foreign body may also be responsible.

Diagnosis:

- CT scan or MRI.
- Bronchoscopy is also helpful.

FIBROSIS OF LUNG

Instruction by the examiner:

- Examine the chest for respiratory system. Or, examine the front of the chest.

Presentation of a Case (Supposing Left Sided):

- There is flattening of upper part of chest, crowding of ribs, drooping of the shoulder.
- Plus, other findings as in collapse (see collapse of the lung).

My **differential diagnoses** are:

- Fibrosis of the left lung.
- Collapse of the left lung.

Q: What is the **more likely** diagnosis in this case? **Why?**

A: Fibrosis of the left lung, because there is flattening of upper part of chest, crowding of ribs, drooping of the shoulder, which indicates fibrosis (i.e., a chronic process).

Q: Can it be **collapse** also?

A: Yes, if it is longstanding or chronic.

Q: What are the **causes** of fibrosis?

A: Localized fibrosis may occur in:

- Upper lobe: TB (commonest).
- Lower lobe: Bronchiectasis (commonest).

Causes of upper lobe (zone) fibrosis—mnemonic: SCHAT

- **S:** Silicosis, sarcoidosis.
- **C:** Coal worker's pneumoconiosis.
- **H:** Histiocytosis (Langerhans cell histiocytosis) and histoplasmosis.
- **A:** Allergic bronchopulmonary aspergillosis, ankylosing spondylitis.
- **R:** Radiation (typically in mid zone).
- **T:** TB.

Causes of lower lobe (zone) fibrosis—mnemonic: RASCIO

- **R:** Rheumatoid arthritis.
- **A:** Asbestosis.
- **S:** Scleroderma.
- **C:** Collagen vascular disease.
- **I:** Idiopathic pulmonary fibrosis.
- **O:** Others (drugs: bleomycin, busulphan, nitrofurantoin, methotrexate and amiodarone).



Drooping of left shoulder with flattening of the chest

N.B.: Generalized fibrosis involving both the lungs occur in DPLD.

Q: What are the **types** of fibrosis of the lung?

A: As follows:

- Focal fibrosis due to inhalation of mineral dust (pneumoconiosis).
- Replacement fibrosis (damaged lung tissue replaced by fibrosis), e.g., TB.
- Interstitial fibrosis due to any cause of DPLD (RA, systemic sclerosis or SLE).

Q: What **investigations** should be done in fibrosis of lung?

A: As follows:

- CBC.
- Chest X-ray, PA view.
- CT scan of chest.
- Bronchoscopy if needed.
- Other investigations: according to suspicion of cause.

Q: How to **treat** fibrosis of lung?

A: As follows:

- Treatment according to cause.
- Symptomatic and supportive treatment should be given.

LUNG ABSCESS

Instruction by the examiner:

- Examine the chest for respiratory system.

Presentation of a Case: (Present as in Consolidation).

My diagnosis is **Lung abscess**.

Q: What are the **differential diagnoses**?

A: As follows:

- Consolidation (during resolution stage).
- Bronchiectasis.

Q: Why **not consolidation**?

A: Because in consolidation, there is fever with cough, initially dry but later rusty. Also, clubbing is absent.

Q: Why **it is lung abscess**?

A: Because in lung abscess:

- The patient is toxic with high temperature.
- Clubbing is present, which is against consolidation.
- Cough is purulent with foul smelling purulent sputum.

Q: With these findings, can it be **consolidation only**?

A: Yes, it may be during resolution stage.

Q: Could it be **bronchiectasis**?

A: Yes, because there is clubbing with coarse crepitations. However, in bronchiectasis, crepitations are mostly on the basal area. Also, there is no fever and patient is not toxic (unless there is secondary infection).

Q: What **investigations** should be done in lung abscess?

A: As follows:

- CBC (leucocytosis).
- X-ray chest (cavity with air fluid level).
- Sputum examination: Gram staining, C/S (both aerobic and anaerobic), AFB, fungus, malignant cells.
- CT or MRI (in some cases).
- Bronchoscopy (to exclude mass and foreign body).
- Blood sugar.

READ THE FOLLOWING TOPICS IN RELATION TO LUNG ABSCESS

Q: What is **lung abscess**? What are the **causes**?

A: It is a localized area of suppuration within the lung parenchyma that leads to parenchymal destruction and is manifested radiologically as a cavity with air fluid level (**not due to TB**).

Causes of lung abscess:

- Aspiration of nasopharyngeal or oropharyngeal contents: Such as in vomiting, anaesthesia, tooth extraction, tonsillectomy, unconscious patient, alcoholism and achalasia cardia. Organisms are aerobic and anaerobic.
- Specific infections (*S. pneumoniae* type 3, *S. aureus*, *K. pneumoniae* and fungal). In HIV, *Pneumocystis jiroveci*, *Cryptococcus neoformans* and *Rhodococcus equi*.
- Obstruction by bronchial carcinoma, adenoma and foreign body.
- Infection in pulmonary infarction (by *S. pneumoniae*, *S. pyogenes*, *S. aureus*, *Haemophilus influenzae* and anaerobic).
- Spread from liver abscess and subphrenic abscess (due to transdiaphragmatic spread).
- Haematogenous from other infection as septic emboli (pelvic abscess, salpingitis, right-sided endocarditis, IV drug abuse).
- Lemierre's syndrome is a rare cause of pulmonary abscesses, usual causative agent is *Fusobacterium necrophorum*.

Q: How the patient of lung abscess usually **presents**?

A: As follows:

- Severe cough with profuse foul-smelling sputum, may be foetid (anaerobic).
- Haemoptysis.
- Chest pain (pleuritic).
- Fever, usually high with chill and rigour, with profuse sweating.
- Malaise, weakness and loss of weight.

Q: What are the **physical findings** in lung abscess?

A: It depends on site. If deep seated within the lung parenchyma, there may not be any physical findings. If it is near the surface, findings are:

1. Features of consolidation usually.
2. Rarely, features of cavitation.
3. Sometimes, combined features of consolidation and cavitation, if large abscess.
4. General features are:
 - Patient looks toxic and emaciated.
 - Temperature high.
 - Generalized clubbing.

Q: What are the **characteristics of sputum** in lung abscess?

A: If the sputum is kept in a bottle, there are 3 layers (as in bronchiectasis):

- Lower: Sediment (epithelial debris and bacteria).
- Middle: Thick liquid.
- Upper: Frothy.

Q: What is the **common site** of lung abscess?

A: As follows:

1. Lung abscess is common in right middle lobe.
2. If it is due to aspiration, commonest site depends on the posture of the patient during aspiration.
 - If the patient is lying down: abscess forms in the posterior segment of upper lobe or apical segment of lower lobe.
 - If the patient is in upright position: common site is basal segment.

Q: Why lung abscess is more common on the **right side**?

A: Because, right major bronchus is more vertical than left.

Q: What are the **complications** of lung abscess?

A: As follows:

- Pleurisy.
- Empyema.
- Bronchiectasis.
- Fibrosis.
- Septicaemia.
- Cerebral abscess (common in parietal lobe or posterior frontal region).
- Amyloidosis (rare), in chronic cases.

Q: How to **treat** lung abscess?

A: Sputum is sent for C/S and broad-spectrum antibiotic should be started:

- Clindamycin—600 mg IV every 8 hours until improvement, then 300 mg orally every 6 hours.
- **Or**, Co-amoxiclav orally every 8 hours **Or**, Amoxicillin 500 mg every 8 hours plus metronidazole (500 mg orally or IV every 8 to 12 hours).
- **Or**, cefuroxime 1 g IV 6 hourly **plus** metronidazole 500 mg IV 8 hourly for 5 days, followed by cefaclor **plus** metronidazole (in 70% cases anaerobic organisms are present, but mixed organisms are also common).
- In case of MRSA, Vancomycin 15 mg/kg IV every 12 hours **Or**, Linezolid 600 mg IV every 12 hours.
- High dose penicillin is usually given for *Actinomyces*.
- If improves, continue the therapy.
- If no response to empirical therapy: antibiotic should be given according to C/S finding.
- Treatment should be continued for 4 to 6 weeks.
- Patient with lung abscesses should be treated until radiographic resolution of the abscess cavity occurs.
- Postural drainage and chest physiotherapy.
- If no response to medical therapy (which may occur in 1 to 10% cases) then, percutaneous aspiration should be done (USG or CT guided).
- Sometimes, surgery (lobectomy) may be done.
- Treatment of the cause, if present.
- General measures for fever, weakness, dehydration etc.

Q: What are the indications of surgery in lung abscess?

A: As follows:

- No response to medical therapy.
- Increasing size of the abscess.
- Massive haemorrhage or haemoptysis.
- Suspected neoplasm.
- Congenital lung malformation.

Q: What are the other causes of cavitory lesions in the lung?

A: As follows:

- Tuberculosis.
- Cavitating bronchial carcinoma (squamous).
- Pulmonary infarction.
- Fungal infection (histoplasmosis).
- Wegener's granulomatosis.
- Rheumatoid nodules.
- Consolidation (*St. pneumoniae* serotypes 3).

Q: What are the causes of multiple cavitory lesions in the lung?

A: As follows:

- Tuberculosis.
- Staphylococcal lung abscess (in children).
- Fungal infection.
- Klebsiella.
- Amoebiasis.

Q: What are the causes of multiple lung abscess?

A: As follows:

- Aspiration of infected material.
- *S. aureus* (in children).
- Klebsiella infection.
- Fungal infection.
- Amoebiasis.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Instruction by the examiner:

- Examine the chest for respiratory system.

Presentation of a Case:

On inspection:

- The patient is dyspnoeic with pursing of lips, respiratory rate is 30/min.
- Chest is barrel shaped with indrawing of lower intercostal space on inspiration (due to low flat diaphragm).
- There is suprasternal and supraclavicular space excavation with prominent accessory muscles of respiration.

On palpation:

- Trachea is central, tracheal tug is present (descent of trachea during inspiration).
- Cricosternal distance (distance between suprasternal notch and cricoid cartilage) is reduced (normally 3 fingers or more).
- Apex beat is not felt.
- Chest expansion is reduced and chest movement is vertical.
- Vocal fremitus is reduced on both sides.

On percussion:

- Increased resonance or hyperresonance in both lung fields.
- Obliteration of liver and cardiac dullness (liver dullness may be lower down).

On auscultation:

- Breath sound is diminished vesicular with prolonged expiration.
- Few rhonchi are present (mention, if any).
- Vocal resonance is normal.

My diagnosis is **COPD**.

Q: What is your **differential diagnosis**?

A: As follows:

- Chronic, severe or persistent bronchial asthma.
- Chronic bronchitis with emphysema.

Q: What is the basic **difference** between bronchial asthma and COPD?

A: Bronchial asthma is reversible, but COPD is not fully reversible and is progressive.

Q: How to **confirm** COPD?

A: By spirometry and reversibility test.

Q: What are the **findings** in spirometry?

A: As follows:

- $FEV_1 < 80\%$ predicted.
- $FEV_1 : FVC < 70\%$ predicted.
- Bronchodilator reversibility test shows $< 15\%$ increase in FEV_1 after giving bronchodilator.

Q: What investigations should be done in COPD?**A:** As follows:

1. CBC (polycythaemia and increased PCV due to persistent hypoxaemia).
2. Chest X-ray PA view (shows increased translucency, low flat diaphragm, tubular heart, widening of intercostal space).
3. ECG (usually normal. In cor pulmonale, there may be features of right ventricular hypertrophy).
4. Echocardiogram (may show features of cor pulmonale).
5. Lung function tests:
 - FEV₁ and FVC are reduced. Ratio of FEV₁:FVC is also reduced (indicates obstructive airway disease).
 - Post-bronchodilator FEV₁ < 80% predicted value and FEV₁/FVC is < 70%.
 - Other tests: Lung volumes may be normal or increased. Carbon monoxide transfer factor is low (in emphysema).
6. PEF (reduced).
7. Blood gas analysis:
 - Often normal at rest.
 - PO₂ (reduced).
 - PCO₂ (normal or increased).
 - pH (acidosis).
8. HRCT (to assess COPD, characters of emphysema, particularly bullae).
9. Sputum examination (if infection).
10. α₁-antitrypsin level: May be done in young, non-smoker patient with basal emphysema.

READ THE FOLLOWING TOPICS IN RELATION TO COPD
Q: What is COPD?

A: Chronic obstructive pulmonary disease is a preventable and treatable disease characterized by persistent airflow limitation that is usually progressive, and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. It is diagnosed by history and spirometry. Post-bronchodilator shows FEV₁ < 80% predicted and FEV₁:FVC < 70% predicted.

Q: What are the mechanisms of airflow limitation in COPD?**A:** As follows:

- Increased mucus production and reduced mucociliary clearance.
- Loss of elastic recoil.
- Increased muscle tone.
- Pulmonary hyperinflation.

Q: What are the presentations of COPD?**A:** Usually the patient is above 40 years, male and smoker. Features are:

- Chronic cough and sputum production, which is progressively increasing.
- Progressively increasing breathlessness.
- There may be haemoptysis and morning headache (due to hypercapnia).

Q: What are the systemic features in COPD?

A: Muscular weakness, peripheral oedema due to impaired salt and water excretion, weight loss due to altered fat metabolism, increased osteoporosis, increased circulating inflammatory markers.

Q: What are the risk factors or causes of COPD?

A: Multiple factors are responsible for COPD, such as:

1. Exposure to:
 - Smoking (commonest): Active or passive.
 - Indoor and outdoor air pollution.
 - Occupation: Exposure to dust, fumes, smokes, chemicals etc. (e.g., coal miners and those who work with cadmium).
 - Urban dweller.
 - Low socio-economic status.
 - Low birth weight.
 - Poor lung growth that may be due to childhood infections or maternal smoking.
 - Infections: Recurrent lung infection, persistent adenovirus in lung tissue, HIV infection is associated with emphysema.
 - Cannabis smoking (controversial).
2. Host factors:
 - Genetic factors: α_1 -antitrypsin deficiency.
 - Airway hyper-reactivity.
 - More in male and Caucasians.
 - Biofuel mass.

Q: What organisms are associated with acute exacerbation of COPD?

A: Common organisms: *Haemophilus influenzae* and *S. pneumoniae*. Other less common organisms are *Moraxella catarrhalis*, *Chlamydia pneumoniae* and *Pseudomonas aeruginosa*.

Q: What are the stages or classification of COPD?

A: According to the GOLD criteria, COPD is classified as follows:

Stage	Spirometry	Symptoms
0. At risk	Normal.	Presence of chronic symptoms (cough, sputum production).
I. Mild	FEV1/FVC <70%. FEV1 $\geq$ 80% predicted.	None or mild.
II. Moderate	FEV1/FVC <70%. FEV1 50 to 79% predicted.	Mild-to-moderate symptoms.
III. Severe	FEV1/FVC <70%. FEV1 30 to 49% predicted.	Breathlessness on minimal exertion, e.g., dressing.
IV. Very severe	FEV1/FVC <70%. FEV1 <30% predicted or FEV1 <50% predicted plus chronic respiratory failure	Breathlessness at rest.

Q: What are the complications of COPD?**A:** As follows:

- Pulmonary hypertension.
- Cor pulmonale.
- Respiratory failure.
- Secondary infection.
- Polycythaemia.

Q: How to manage COPD?**A:** As follows:

1. Smoking must be stopped, avoidance of dust, fume, smoke etc.
2. Drug therapy according to the stage:

I. Mild	Avoidance of risk factors. • Short-acting inhaled bronchodilator like β_2 agonist (salbutamol, terbutaline) or anticholinergic (ipratropium) when needed.
II. Moderate	Above treatment plus: • Regular treatment with one or more long-acting bronchodilator: β_2 agonist (e.g., salmeterol, formoterol) or anticholinergic (tiotropium) when needed. • Rehabilitation.
III. Severe	Above treatment plus: • Inhaled steroid (fluticasone).
IV. Very severe	Above treatment plus: • Longterm oxygen, if chronic respiratory failure. • Surgical treatment, if needed.

3. Other therapy:

- Oxygen, if needed.
- Mucolytic (N-acetylcysteine).
- Antibiotic (if infection).
- Diuretic (if oedema).
- Pulmonary rehabilitation.
- Influenza and pneumococcal vaccination.
- Reduction of obesity.

4. Surgical intervention:

- Bullectomy: If young patient, large bulla compressing surrounding lung tissue, no generalized emphysema.
- Lung volume reduction surgery (LVRS): Predominant upper lobe emphysema, preserved gas transfer and no evidence of pulmonary hypertension.
- Lung transplantation.

Q: What is the role of inhaled steroid in COPD?

A: Inhaled steroid is recommended for symptomatic patient with moderate to severe COPD and also with frequent exacerbations but not in mild COPD. It reduces the frequency and severity of exacerbation. There is small improvement of FEV_1 , but it does not alter the natural history of FEV_1 decline.

Q: How **domiciliary oxygen** is given? What is the **aim** of the therapy?

A: O₂ is given 2 to 4 L/min for 15 h/day by nasal prongs. The aim is to increase the PaO₂ to at least 8 kPa (60 mmHg) at sea level during rest or SaO₂ to at least 90%. (Greater benefit may be seen in patients who receive > 20 h/day).

Q: What are the indications of **long term domiciliary oxygen therapy** in COPD?

A: As follows:

1. PaO₂ < 7.3 kPa (55 mmHg) irrespective of PaCO₂ and FEV1 < 1.5 L.
2. PaO₂ 7.3 to 8 kPa (55 to 60 mmHg) associated with:
 - Pulmonary hypertension.
 - Peripheral oedema.
 - Nocturnal hypoxaemia.
 - Secondary polycythaemia.
3. Carboxyhaemoglobin < 3% (in patient who have stopped smoking).
4. Terminally ill patient of whatever the cause with PaO₂ < 7.3 KPa.

N.B.: Arterial blood gases should be measured in clinically stable patients on optimal medical therapy on at least two occasions, 3 weeks apart.

Q: Why **low concentration O₂** is given in COPD? Or what happens when **high-flow O₂** is given?

A: In COPD, the patient is dependent on hypoxic drive. Low-flow oxygen is due to its effect in the chemo-responsiveness of the respiratory centre in the medulla (part of the brainstem). High-flow oxygen blunts responsiveness of the respiratory centre in the medulla and causes carbon dioxide retention, so aggravates respiratory failure (type 2 respiratory failure).

Q: What is the role of **oral steroid** in COPD? What is the **indication** of steroid in COPD?

A: Oral steroid is useful during exacerbation, but maintenance therapy should be avoided. Indications are:

- Stage III or IV disease.
- In stage II, if oral steroid trial shows responsiveness.
- Severe exacerbations of COPD.
- Frequent episodes of exacerbations.

N.B.: Regarding air travel:

- *Pre-flight assessment should be done by spirometry and hypoxic challenge test with 15% oxygen. If saturation is maintained > 90%, the patient can be allowed to travel. If not, air travel should be avoided or undertaken only with inspired oxygen therapy.*
- *Sufficient supplementary oxygen should be given during flight to keep the PaO₂ above 50 mmHg, which is achieved by increasing the flow by 1 to 2 L/min.*
- *Patients who use to take continuous oxygen at home will require this supplementation.*

Q: What is the prognosis of COPD?**A:** Prognosis of COPD is predicted by **BODE** index:

Variable	Points on BODE index			
	0	1	2	3
1. Body mass index	>21	≤21		
2. Obstruction to airflow (FEV ₁ % predicted)	≥65	50–64	36–49	≥35
3. Dyspnoea (MMRC scale)	0–1	2	3	4
4. Exercise capacity (metres walked in 6 min)	≥350	250–349	150–249	≤149

4-year mortality rate for BODE index 0 to 2 is 10%, whereas that of BODE index 7 to 10 is 80%.

N.B.: Poor prognostic factors are advancing age (inversely related), fall of FEV₁ over time, weight loss and pulmonary hypertension.

Q: How to manage acute exacerbation of COPD (type II respiratory failure)?**A:** As follows:

- Oxygen: Continuous low concentration oxygen via Venturi mask to raise PaO₂ > 8 kPa (60 mmHg). Initially 24 or 28% oxygen is given and increased gradually, provided PaCO₂ does not rise unacceptably. If PaCO₂ rises and pH falls below 7.25, artificial ventilation or a respiratory stimulant should be given.
- Bronchodilator: Nebulized short acting β₂-agonist (e.g., salbutamol) with an anticholinergic agent (e.g., ipratropium).
- Oral prednisolone 30 mg daily for 10 days.
- Antibiotic: Given if infection.
- Diuretic: If peripheral oedema.
- Chest physiotherapy. Secretions should be removed by suction.
- Respiratory support: If above treatment fails or there is tachypnoea and acidosis (pH < 7.35). Non-invasive ventilatory technique like BiPAP is used first. CPAP is occasionally needed.
- Respiratory stimulant: Less used. Doxapram 1.5 to 4.0 mg/min by slow IV infusion may be helpful.

Indications of hospitalization are:

- Severe symptoms or acute worsening that fails to respond to outpatient management.
- Presence of cyanosis.
- Peripheral oedema.
- Alteration of consciousness.
- Comorbidity and poor social circumstances.

Q: What are the **discharge criteria** of COPD patient?

A: As follows:

- The patient is clinically stable and no parenteral therapy should be there for 24 h.
- Inhaled bronchodilators are required less than 4 hourly.
- Oxygen delivery has ceased for 24 h.
- The patient is able to eat and sleep without significant episodes of dyspnoea.
- The patient or caretaker understands and is able to administer medications.
- Follow-up and home care arrangements (e.g., home oxygen, home care, Meals on Wheels, community nurse, allied health, general practitioners and specialist) have been completed.
- If previously able, the patient is ambulating safely and independently and performing activities of daily living.

CHRONIC BRONCHITIS

Instruction by the examiner:

- Examine the chest for respiratory system.

Presentation of a Case:

Inspection:

- Shape of the chest: Normal.
- Movement of the chest: Bilaterally restricted.
- Intercostal space: Appears full.

Palpation:

- Trachea: Central.
- Apex beat: In the left fifth intercostal space in the mid-clavicular line.
- Chest expansion: Reduced.
- Vocal fremitus: Normal.

Percussion:

- Percussion note: Normal resonance.
- Area of liver dullness: In the right fifth intercostal space in mid-clavicular line.
- Area of cardiac dullness: Impaired.

Auscultation:

- Breath sounds: Vesicular with prolonged expiration.
- Added sounds: Plenty of rhonchi in both lung fields, which are present in both inspiration and expiration.
- Vocal resonance: Normal.

FET (forced expiratory time): 8 s (normally <6 s)

My diagnosis is **Chronic bronchitis**.

*N.B.: In many cases, signs of emphysema and chronic bronchitis may be present together. Then, the diagnosis is **chronic bronchitis with emphysema**.*

Q: What are your **differential** diagnoses?

A: As follows:

- Chronic persistent bronchial asthma.
- COPD.
- Bilateral extensive bronchiectasis.
- Chronic LVF.

Q: What is **chronic bronchitis**?

A: It is defined clinically as ‘the presence of cough, productive of sputum, not attributable to other causes, on most of the days, for 3 consecutive months, at least for 2 successive years’.

Q: What are the causes of chronic bronchitis?**A:** Multiple factors are responsible:

- Smoking.
- Exposure to dust, fume, foggy environment (may be occupational). Dampness, sudden change in temperature—all exaggerate chronic bronchitis.
- Infection (*H. influenzae*, *S. pneumoniae*, *Moraxella catarrhalis*: All of these exaggerate chronic bronchitis).

Q: How does the patient present with chronic bronchitis?**A:** It is common in smokers. Usual presentations are:

- Cough with sputum: Cough is more marked in the morning, also on exposure to cold and during winter.
- The sputum is mucoid or mucopurulent, usually not associated with haemoptysis.
- Tightness of the chest and breathlessness on exertion.
- In advanced stage, features of pulmonary hypertension and cor pulmonale are present.
- The patient looks as blue bloater (cyanosed and oedematous).

Q: What are the complications of chronic bronchitis?**A:** As follows:

- Respiratory failure—both type I and type II.
- Emphysema.
- Secondary polycythaemia.
- Secondary infection.
- Pulmonary hypertension.
- Cor pulmonale.

Q: What investigations should be done in chronic bronchitis?**A:** As follows:

1. CBC.
2. Chest X-ray PA views (no significant abnormality).
3. ECG (Usually normal. In cor pulmonale, there is RVH).
4. Lung function tests:
 - FEV₁ (reduced).
 - FVC (reduced).
 - Ratio of FEV₁:FVC is also reduced (indicates obstructive airway disease).
 - Other tests: Residual volume (RV) is increased, total lung capacity (TLC) is increased, gas transfer (either normal or mildly reduced).
5. PEF (reduced).
6. Blood gas analysis:
 - PO₂ (reduced).
 - PCO₂ (normal or increased).
 - pH (acidosis).
7. CT scan in some cases.

Q: How to treat chronic bronchitis?**A:** As follows:

1. Smoking must be stopped.
2. Avoid air pollution (dust, fume).
3. Control of infection with appropriate antibiotic.
4. Bronchodilator:
 - Inhaled β -agonist: Salbutamol (200 μ g 4 to 6 hourly), terbutaline.
 - Inhaled antimuscarinic: Ipratropium (40 μ g 4 hourly), tiotropium (18 μ g daily), oxitropium (200 μ g BD).
 - Long-acting β -agonist: Salmeterol, formoterol.
 - Oral theophylline (in some cases).
5. Inhaled corticosteroid: beclomethasone (400 μ g BD) or budesonide or fluticasone. In severe case, oral prednisolone 30 mg for 2 weeks, followed by maintenance dose.
6. Mucolytic agents like bromhexine or *N*-acetylcysteine (200 mg 8 hourly orally for 8 weeks) may be given.
7. Other measures:
 - Chest physiotherapy.
 - Exercise and weight reduction, if obese.
 - Long-term domiciliary oxygen.
 - Pulmonary rehabilitation.
 - Annual influenza vaccine, 5 yearly pneumococcal vaccine and *Haemophilus influenzae* vaccine may be given.

Q: How to treat acute exacerbations?**A:** As follows:

- Nebulized bronchodilators (such as terbutaline, ipratropium bromide).
- Antibiotic to control infection.
- Oxygen inhalation (24%, 1 to 3 L/min).
- IV hydrocortisone initially. When the condition is improved, oral steroid may be given
- Steroid is only used in acute exacerbations and unlike in asthma, it does not influence the course of chronic bronchitis.

EMPHYSEMA

Instruction by the examiner:

- Examine the chest for respiratory system.

Presentation of a Case:

Inspection:

- Chest is barrel shaped.
- Indrawing of the lower intercostal space on inspiration (due to low, flat diaphragm).

Palpation:

- Trachea is central, tracheal tug (descent of trachea during inspiration) is present.
- Cricosternal distance (distance between suprasternal notch and cricoid cartilage): Reduced (normally 3 fingers or more).
- Apex beat is not felt.
- Chest expansion is reduced (tell in centimetre).
- Vocal fremitus is reduced.

Percussion:

- Hyperresonance in both lung fields.
- Obliteration of liver and cardiac dullness (liver dullness may be lowered down).

Auscultation:

- Breath sound: Diminished vesicular with prolonged expiration.
- Vocal resonance is reduced.

My diagnosis is **Emphysema**.

*N.B.: If rhonchi are present in both lung fields with above findings, diagnosis is **Chronic bronchitis with emphysema**.*

Q: What investigations should be done in emphysema?

A: As follows:

1. X-ray chest P/A view (it shows the following features of emphysema):
 - Increased translucency of both lung fields with loss of peripheral vascular markings.
 - Low, flat diaphragm.
 - Tubular heart.
 - Widening of intercostal space and ribs appear horizontal.
 - Bulla may be present (which is pathognomonic).
 - Prominent pulmonary arterial shadow in both hilum (due to pulmonary hypertension).
2. Lung function tests:
 - FEV₁ and FVC are reduced. Ratio of FEV₁:FVC is reduced (obstructive type).
 - Postbronchodilator FEV₁ is <80% predicted and ratio of FEV₁:FVC is <70% predicted.
 - PEF: Reduced.
 - Lung volume with increased TLC and RV.

3. Arterial blood gas analysis:
 - Low PCO_2 (due to hyperventilation).
 - Low PO_2 .
 - Impaired gas transfer of CO.
4. Other investigations:
 - CBC with ESR (polycythaemia may be present).
 - CT scan of the chest (HRCT): Highly suggestive.
 - To confirm: Biopsy of the lung tissue (not a routine test).
 - In young patient: serum level of α_1 -antitrypsin may be done.
 - ECG may show tall P, right ventricular hypertrophy, right axis deviation in patient with cor pulmonale.
 - Echocardiography.

Q: What is the **definitive diagnosis** of emphysema?

A: Histopathological (but not done routinely).

READ THE FOLLOWING TOPICS IN RELATION TO EMPHYSEMA

Q: What is **emphysema**?

A: It is the permanent distension of alveoli with destruction of their walls distal to the terminal bronchioles.

Q: What are the **presentations** of emphysema?

A: Breathlessness on exertion and minimum cough with lip pursing.

Q: What are the **types** of emphysema?

A: 4 types:

- Centriacinar: Involves the proximal part of acini, limited to respiratory bronchiole with relatively less change in acinus.
- Panacinar: All the alveoli and alveolar ducts in acinus are involved, both central and peripheral portion. It occurs mostly in α_1 -antitrypsin deficiency.
- Paraseptal: Along the septa, blood vessels and pleura.
- Scar or irregular emphysema: Scarring and damage affecting the lung parenchyma without involving acinus structure.

Q: What are the **causes** of emphysema?

A: As follows:

- Smoking.
- Cold, dust (centrilobular).
- α_1 -antitrypsin deficiency.
- Macleod syndrome (unilateral emphysema).

Q: How **smoking** causes emphysema?

A: Some mechanisms are responsible:

- Prolonged smoking causes inflammation in airways, release of oxidants and proteinase from inflammatory cells, which are responsible for irreparable damage to supporting connective tissue of alveolar septa.
- There is increased proteinase synthesis, but also inactivation of antiproteinase by excess production of enzymes. As a result, there is imbalance between proteinase and antiproteinase.

Q: Why lip pursing in emphysema?

A: By this in expiration through partly closed lips, there is increased end-expiratory pressure that keeps airway open, helping to minimize air trapping.

Q: What are the complications of emphysema?

A: As follows:

- Pulmonary hypertension.
- Cor pulmonale.
- Respiratory failure type 1.
- Bullae, which may rupture causing pneumothorax.
- Secondary infection.
- Polycythaemia.

Q: What are the signs of emphysema?

A: As follows:

- The patient is dyspnoeic with lip pursing.
- Barrel-shaped chest.
- Supra-sternal and supra-clavicular excavation during inspiration.
- Prominent sternomastoid and scalene muscles.
- Tracheal tug.
- Reduced crico-sternal distance (length of trachea above supra-sternal notch).
- Indrawing of lower intercostal space during inspiration.
- Horizontal ribs with wide intercostal spaces.
- Wide subcostal angle.
- Obliteration of liver and cardiac dullness.



Lip pursing

Q: What is bullae? What are the causes? What is the treatment?

A: It is the thin-walled air space produced by rupture of alveolar walls. Bullae may be single or multiple, large or small, and usually associated with emphysema. It is usually situated subpleurally. Rupture may lead to pneumothorax. Large bullae may compress the lung tissue and impair lung function.

The causes of bullae are:

- Emphysema.
- Congenital (rare).

Treatment:

- Small bullae: No treatment, treatment of primary cause.
- Large bullae with impaired lung function require surgical ablation of bullae.

Q: How to treat emphysema?**A:** As follows:

1. General treatment:
 - Smoking must be stopped.
 - Weight reduction, if obese.
 - Exercise.
2. For breathlessness:
 - Inhaled salbutamol (200 µg 4 to 6 hourly) or ipratropium (40 µg 4 hourly) or tiotropium (18 µg daily) or oxitropium (200 µg BD).
 - If no response, inhaled corticosteroid beclomethasone (400 µgm BD).
 - In severe case, oral prednisolone 30 mg for 2 weeks, followed by maintenance dose.
3. Antibiotic, if secondary infection.
4. In chronic cough: Mucolytic therapy (N-acetylcysteine 200 mg 8 hourly orally for 8 weeks).
5. Domiciliary O₂ may be given.
6. Vaccination: yearly influenza vaccine, 5 yearly pneumococcal vaccine. *Haemophilus influenzae* vaccine may be given.
7. Other treatment:
 - α₁-antitrypsin in case of deficiency.
 - Lung transplantation in young patient.
 - Surgical intervention (if large bullae).

Q: What is pink puffer and blue bloater?**A:** As follows:**Pink puffer:**

- The patient is not cyanosed (pink), but dyspnoeic with lip pursing (puffer). No oedema.
- Usually lean and thin, 50 to 75 years of age.
- It is found in emphysema, commonly panacinar.
- Usually there is no cor pulmonale.
- Exertional dyspnoea is the main feature and cough less common.
- Arterial PO₂ and PCO₂ are relatively normal.

Blue bloater:

- The patient is cyanosed (blue) and oedematous (bloater). But not dyspnoeic (or mild dyspnoea).
- It is found in chronic bronchitis, age 40 to 45 years. Oedema is due to cor pulmonale.
- Cough with sputum is the main feature, dyspnoea is less common.
- Pulmonary hypertension, right ventricular hypertrophy, cor pulmonale and secondary polycythaemia may develop (patient may appear plethoric).
- There is marked arterial hypoxaemia and hypercapnia (low PO₂ and increased PCO₂).

Q: What are the restrictive airway disease and obstructive airway disease?**A:** As follows:

- Restrictive: DPLD, ankylosing spondylitis and kyphoscoliosis.
- Obstructive: Emphysema, chronic bronchitis and bronchial asthma.

Q: What are the **differences between restrictive and obstructive** airway disease?

A: As follows:

Points	Restrictive	Obstructive
1. FEV ₁ and FVC	Proportionately reduced.	FEV ₁ is markedly reduced and FVC also reduced.
2. FEV ₁ :FVC	Normal.	Reduced.
3. RV	Reduced or normal.	Increased.
4. TLC	Reduced.	Increased.
5. RV:TLC	Normal or slightly increased.	Markedly increased.

N.B.: Both TLCO and transfer coefficient of carbon monoxide (K_{CO}) are reduced in restrictive and obstructive airway disease.

MASS LESION IN LUNG (BRONCHIAL CARCINOMA)

Mass lesion in lung may be isolated bronchial carcinoma without definitive signs. There may be collapse or pleural effusion, or SVC obstruction and radiation mark in chest.

Instruction by the examiner:

- Examine the chest for respiratory system.

N.B.: The patient is middle-aged or elderly, emaciated or cachexic with generalized clubbing and nicotine stain in fingers.

Presentation of a Case: (Supposing Right-sided Lesion)

On inspection:

- Restricted movement of upper part of chest.
- There is radiation mark on the chest (if any).

On palpation:

- Trachea: Central and apex beat in normal position.
- Vocal fremitus: Reduced or absent (rib tenderness may be present).

On percussion:

- Dullness in right upper part of chest (mention the space).

On auscultation:

- Breath sound is reduced or absent.
- Vocal resonance is reduced or absent.

My diagnosis is **Mass lesion in the lung, more likely Bronchial carcinoma.**

Q: Why it is bronchial carcinoma?

A: Because:

- Elderly patient, grossly emaciated.
- Presence of generalized clubbing with nicotine stain, may be hypertrophic osteoarthropathy.
- Radiation mark in the chest.

Q: What relevants do you like to see?

A: As follows:

- Hands: Clubbing with nicotine stain, hypertrophic osteoarthropathy, wasting of small muscles of hand (due to involvement of lower trunk of brachial plexus).
- Supraclavicular, axillary lymph nodes (metastasis).
- Eye: Horner's syndrome (in Pancoast tumour).
- Evidence of SVC obstruction.



Bronchial carcinoma (emaciated with prominent vein)

Q: What will you see in **the eyes** of the patient?

A: I will look for partial ptosis, miosis and enophthalmos, which indicates Horner's syndrome, found in Pancoast tumour.

Q: What are the **differential diagnoses**?

A: As follows:

- Pleural effusion.
- Pulmonary tuberculosis.
- Other mass lesions (neurofibroma, dermoid cyst, hydatid cyst).

Q: Why **not this is pleural effusion**?

A: In pleural effusion, trachea and apex beat are shifted to the opposite side.

Q: Why **not this is collapse**?

A: In collapse, trachea and apex beat are shifted to the same side.

Q: Why **not consolidation**?

A: In consolidation, there is bronchial breath sound and increased vocal resonance.

Q: What are the **causes or risk factors** of bronchial carcinoma?

A: As follows:

- Smoking is the major risk factor. Even passive smoking causes 1.5 times increase in the risk of bronchial carcinoma.
- Other factors are exposure to asbestos, silica, beryllium, cadmium, chromium, arsenic, iron oxide, radon, radiation, petroleum products and oils, coal tar, products of coal combustion.
- Adenocarcinoma may develop in non-smokers and in old scar.
- DPLD (previously called ILD).

Q: What are the **types** of bronchial carcinoma?

A: 2 types:

- Non small-cell lung carcinoma in 80% (NSCLC).
- Small-cell lung carcinoma in 20% (SCLC). It is also called oat cell carcinoma.

Q: What are the **histological types** of bronchial carcinoma?

A: As follows:

1. Non small-cell: 3 types
 - Squamous-cell carcinoma in 35%.
 - Adenocarcinoma in 30%.
 - Large-cell carcinoma in 15%.
2. Small-cell carcinoma in 20%.

Features of Adenocarcinoma:

- 30% of bronchial carcinoma.
- Arises from mucous cells in the bronchial epithelium.
- Occurs in the periphery of lung.
- Usually develops in or around old scar.
- More in elderly.

- More in female.
- More in non-smoker (Increasing incidence possibly linked to low-tar cigarettes).
- More in far East.
- More in asbestosis.
- Invasion to pleura and mediastinal lymph nodes is common.
- Metastasis to brain, bone and adrenal gland, pleura, lymph nodes is common (distal metastasis is common).
- Most common in USA.

Features of small-cell carcinoma:

- 20 to 30% of bronchial carcinoma.
- Arises from endocrine cells called Kulchitsky cells. These cells are members of amine precursor uptake decarboxylase (APUD) system, which secretes many polypeptide hormones. Some of these hormones act as autocrine fashion, cause cell growth.
- Highly malignant, rapidly growing, early metastasis and inoperable at presentation.
- Usually responds to chemotherapy and radiotherapy, less likely to be cured by surgery.
- Overall prognosis is poor. Survival is short, 3 months to 1 year.

Features of squamous cell carcinoma:

- 35% of bronchial carcinoma.
- Common cell type in Europe.
- Arise from epithelial cells, associated with production of keratin.
- Occasionally cavitate with central necrosis.
- Cause obstructing lesions of bronchus with post-obstructive infection.
- Local spread common, metastasize relatively late.

Features of large cell carcinoma:

- 10 to 15% of bronchial carcinoma.
- Often poorly differentiated.
- Metastasize relatively early.

Features of bronchoalveolar cell carcinoma:

- Found in 1 to 2% of bronchial carcinoma.
- Occurs as peripheral solitary nodule or diffuse nodular lesion of multi-centric origin.
- It may be associated with profuse mucoid sputum expectoration.

Q: What is Pancoast tumour and Pancoast syndrome?

A: As follows:

- **Pancoast tumour:** It is the tumour that arises from apex of the lung. Horner's syndrome may occur due to involvement of the sympathetic pathway as it passes through T1 root (characterized by ipsilateral partial ptosis, enophthalmos, miosis and anhydrosis of the face).

- **Pancoast syndrome:** It is characterized by pain in the shoulder or inner aspect of arm along the ulnar nerve distribution due to involvement of lower part of brachial plexus (C8, T1 T2), wasting of small muscles of hand due to C8 and T1 nerve involvement. Local invasion by the tumour may cause pain and tenderness of 1st and 2nd ribs with rib destruction radiologically. In Pancoast syndrome, treatment is combined surgery and radiotherapy.

Q: What are the **presentations** of bronchial carcinoma?

A: Usually in elderly patient with history of smoking.

1. Due to lung lesion:

- Cough: Dry or sputum production. Changing pattern of regular cough in a smoker is highly suspicious. Bovine cough due to left recurrent laryngeal nerve palsy.
- Haemoptysis: Common in central lesion. Involvement of large blood vessels causes massive haemoptysis.
- Breathlessness (due to bronchial obstruction, collapse, or massive pleural effusion. Involvement of phrenic nerve causes diaphragmatic palsy).
- Chest pain (due to involvement of pleura, rib or chest wall, intercostal nerve or brachial plexus).
- Recurrent pneumonia at the same site or pneumonia with slow resolution is highly suspicious.
- Apical tumour (Pancoast tumour or Pancoast syndrome).

2. Due to local spread in mediastinum:

- Hoarseness of voice and bovine cough (due to involvement of left recurrent laryngeal nerve by left hilar lesion).
- Dysphagia (due to oesophageal obstruction).
- SVC obstruction (with right sided mass or mediastinal lymphadenopathy).
- If pericardium is invaded, there may be pericardial effusion, even cardiac tamponade or arrhythmia.
- Stridor, when lower trachea, carina and main bronchi are narrowed by primary tumour or compression by subcarinal and paratracheal lymph nodes.

3. Distant metastasis (in liver, brain, bone, adrenal, contralateral lung, lymph nodes. Metastasis is common in adenocarcinoma).

4. Nonmetastatic–extrapulmonary manifestations (see below).

5. General features of malignancy: Anorexia, weight loss, malaise, fatigue.

Nonmetastatic extra-pulmonary manifestations (paraneoplastic syndrome):

Occur in 15 to 20% cases of bronchial carcinoma due to secretory products by the tumour. These may precede, coincide or follow after the cancer. Treatment of carcinoma improves the features.

1. Endocrine (10%, usually in small-cell carcinoma):

- SIADH (syndrome of inappropriate ADH, usually in small-cell carcinoma).
- ACTH secretion causing Cushing syndrome (usually in small-cell carcinoma).
- Carcinoid syndrome (usually in small-cell carcinoma).
- Hypercalcaemia due to release of parathormone-like substance (usually in squamous-cell carcinoma).
- Gynaecomastia due to excess oestrogen (in large cell).
- Rarely, hypoglycaemia and thyrotoxicosis.

2. **Neurological** (in any type):
 - Encephalopathies, including subacute cerebellar degeneration.
 - Peripheral neuropathy (usually sensori-motor).
 - Cortical degeneration (dementia).
 - Myelopathy (motor neuron disease).
 - Retinal blindness (in small-cell carcinoma).
3. **Musculoskeletal**:
 - Polymyositis or dermatomyositis (in all types).
 - Myasthenic myopathic syndrome (called Eaton–Lambert syndrome).
 - Clubbing and hypertrophic osteoarthropathy (in non-small-cell type).
4. **Haematological** (in all types):
 - Migrating thrombophlebitis.
 - Disseminated intravascular coagulation (DIC).
 - Thrombotic thrombocytopenic purpura (TTP).
 - Microcytic and normocytic anaemia, occasionally haemolytic.
 - Eosinophilia.
5. **Heart** (in adenocarcinoma):
 - Marantic endocarditis (non-bacterial, thrombotic or verrucous endocarditis).
6. **Skin** (rare):
 - Acanthosis nigricans.
 - Dermatomyositis.
 - Herpes zoster.
7. **Renal**: Nephrotic syndrome due to membranous glomerulonephritis (rare).
8. **Metabolic** (universal at some stage):
 - Loss of weight.
 - Lassitude.
 - Anorexia.

Q: Why chest pain in bronchial carcinoma?

A: Due to metastasis in the rib or chest wall invasion.

Q: What investigations should be done in bronchial carcinoma?

A: As follows:

1. X-ray chest PA view (homogeneous irregular opacity with **sun-ray** appearance may be seen. There may be collapse, pleural effusion, hilar lymphadenopathy, widening of mediastinum, raised hemidiaphragm, rib erosion or destruction).
2. CT scan of chest (MRI is not helpful for primary lesion).
3. Sputum for malignant cells (exfoliative cytology).
4. CT-guided FNAC.
5. FNAC (or biopsy) of lymph nodes (if present).
6. Fibre optic bronchoscopy and biopsy (or bronchial washing and brushing).
7. PET–CT scan is the investigation of choice (highly sensitive and specific for mediastinal staging).
8. To see evidence of metastasis: USG of whole abdomen, X-ray of skull, isotope bone scan etc. Sometimes, CT scan of chest and abdomen, even MRI may be needed.

9. Endobronchial ultrasound guided FNAC: to visualize and take sample from the majority of mediastinal nodes.
10. Video assisted thoracoscopic surgery.
11. Others:
 - CBC, ESR.
 - If pleural effusion (fluid for malignant cell). Pleural biopsy may also be done.
 - Liver function test, renal function test (before chemotherapy).
 - Pulmonary function test, specially FEV₁ (diffusing capacity of the lung for carbon monoxide below 60% predicted is associated with a mortality rate of 25% due to pulmonary complications).

Q: If sputum shows malignant cells, would you do **bronchoscopy and biopsy**?

A: Yes, to see histological type, which is helpful for therapy and prognosis. If squamous-cell carcinoma, radiotherapy is the treatment. If small-cell carcinoma, chemotherapy is necessary.

Q: Why **bronchoscopy** should be done?

A: Bronchoscopy should be done:

- To see the mass and to take biopsy for tissue diagnosis. This will guide further management.
- If the carcinoma involves first 2 cm of either main bronchus, it indicates that the tumour is inoperable.
- If carina is wide and there is loss of sharp angle of carina, it indicates presence of enlarged mediastinal lymph nodes (may be malignant or reactive). Biopsy can be taken by passing a needle through bronchial wall.
- Vocal cord paralysis on the left indicates left recurrent laryngeal nerve palsy, indicates inoperable.

Q: How to **treat bronchial carcinoma**?

A: As follows:

Non-small-cell carcinoma:

1. Surgery should be done, if the tumour is localized to lobe or segment (curative in stage T₁N₀M₀).
2. In operable disease stages T₁N₀–T₃N₂ (stage I–IIIa), adjuvant radiotherapy and chemotherapy following surgery can improve prognosis.
3. If surgery is not possible, radiotherapy or chemotherapy or combined therapy (chemoradiation) should be given.
 - In squamous-cell type: radiotherapy (indicated in SVC obstruction, repeated haemoptysis and chest pain caused by chest wall invasion or skeletal metastasis).
 - Chemotherapy: Cisplatin (or carboplatin) plus gemcitabine remains the standard treatment. Alternately, particularly in older patients, carboplatin and paclitaxel may be given.
 - Second-line therapy—Docetaxel. Nivolumab has a significantly better survival than docetaxel in advanced disease.
 - Adenocarcinoma: Cisplatin plus pemetrexed or vinorelbine is the most effective combination. 4 cycles every 3 weeks are given.

3. Small-cell carcinoma:

- Even small, metastasis occurs early. Surgery is less helpful. Concurrent chemotherapy and radiotherapy using a combination of cisplatin and etoposide or irinotecan may be given.
- A similar degree of improvement can also be achieved with hyperfractionated radiotherapy.
- Extensive disease can be palliated with the combination of carboplatin and etoposide or irinotecan.

4. Other treatments: These are usually palliative.

- Laser therapy with fiberoptic bronchoscopy.
- Endobronchial therapy: Tracheobronchial stent, cryotherapy, laser, brachytherapy (a radioactive source is placed close to the tumour).
- Radiofrequency thermal ablation (RFT).
- Pleural drainage or pleurodesis (in pleural effusion).
- Drug: Steroid, morphine or diamorphine for pain. Oral candidiasis should be treated.
- Short courses palliative radiotherapy are helpful for bone pain, severe cough or haemoptysis.

Q: What is the role of surgery in lung carcinoma?

A: In non-small-cell carcinoma without metastasis, surgery is the treatment of choice. But it has limited role in small-cell carcinoma, as >90% patients have metastasis at the time of presentation.

Q: What are the contraindications of surgery?

A: As follows:

- Distant metastasis (M_1).
- Invasion of central mediastinal structures including heart, great vessels, trachea and oesophagus (T_4).
- Malignant pleural effusion (T_4).
- Contralateral mediastinal lymph node involvement (N_3).
- $FEV_1 < 0.8$ L.
- Poor general condition, severe or unstable cardiac, or other medical problem.

Q: What is the prognosis?

A: If it is localized and surgical resection is possible, the prognosis is good. Otherwise:

- Non-small-cell carcinoma: 50% 2-year survival without spread, 10% with spread.
- Small-cell carcinoma: Median survival is 3 months if untreated, 1 to 1½ year with treatment.

RFT is helpful in some malignancy such as bronchial carcinoma and hepatocellular carcinoma. It is done by placing special needle into the tumour under guidance of CT scan. Electric current from radiofrequency current generator is passed through the needle, which results in generation of heat causing destruction of tumour. RFT is helpful, if the tumour size is <4 cm. Also, sometimes used in large tumour.

Complications of RFT:

- Bleeding.
- Pneumothorax.
- Skin burn.
- Secondary infection and lung abscess.

Q: What is the role of staging?

A: Staging is done to see the possibility of surgical resection of the carcinoma. TNM staging is done for non-small-cell cancer only. In early stage, surgery may be curative. In advanced stages, surgery may not be possible. Small-cell carcinoma is treated according to whether it is limited or extensive.

TNM classification of lung cancer (it is for non-small-cell carcinoma):

- T: Extent of primary tumour.
- N: Involvement of lymph node.
- M: Presence of distant metastasis.

Stages for T:

- Tx: Positive cytology only.
- T1: <3 cm in diameter.
- T2: >3 cm in diameter or extends to hilar region or invades visceral pleura or partial atelectasis or extends into main bronchus, but remains 2 cm or more distal to carina.
- T3: Involvement of chest wall, diaphragm, pericardium, mediastinum, pleura, total atelectasis, main bronchus <2 cm distal to carina.
- T4: Involvement of heart, great vessels, trachea, oesophagus, malignant effusion, vertebral body, carina. Separate tumour nodules.

Stages for N:

- N0: No nodal involvement.
- N1: Peribronchial, ipsilateral hilar or intra-pulmonary lymph node involvement.
- N2: Ipsilateral, mediastinal or subcarinal.
- N3: Contralateral mediastinal, scalene or supra-clavicular.

Stages for M:

- M0: No distant metastasis.
- M1: Distant metastasis.

Q: Which primary cancers that metastasize to lung?

A: Remember the mnemonic—PUBLIK T

- P—Prostate, pancreas.
- U—Uterus, ovary, urinary bladder.
- B—Breast, bone, bronchus.
- L—Liver (hepatoma).
- I—(Intestine and GIT—stomach, colon, rectum).
- K—Kidney.
- T—Testes, thyroid, teratoma.

LOBECTOMY AND PNEUMONECTOMY

Instruction by the examiner:

- Examine the chest for respiratory system.

Presentation of a Case: (Supposing Right-sided Lesion)

On inspection:

- Scar mark of thoracotomy (mention the site).
- Restricted movement.
- Flattening of upper part of chest.
- Crowding of ribs.

On palpation:

- Trachea: Shifted to the right.
- Apex beat: Shifted to the right (mention the site).
- Vocal fremitus: Reduced.

On percussion:

- Dullness in upper part of chest (mention up to the site . . .).
- Upper border of liver dullness is in the right fourth intercostal space in the midclavicular line.

On auscultation:

- Breath sound: Diminished or absent.
- Vocal resonance: Decreased or absent.

My diagnosis is **Right sided pneumonectomy**.

Q: What are the **differential diagnosis**?

A: As follows:

- Complete collapse.
- Extensive fibrosis.
- Rarely, agenesis of lung.

Presence of scar mark of thoracotomy is against the above differential diagnoses.

N.B.: See the following points:

- *Clubbing with nicotine stain and palpable lymph node indicates the cause is malignancy.*
- *Gross shifting of trachea and apex beat indicates pneumonectomy.*
- *Slight or minimum shifting of trachea and apex beat indicates upper lobectomy. Trachea and apex beat may not be shifted in lower lobectomy.*
- *Breath sound is absent or grossly diminished in pneumonectomy, slightly diminished in lobectomy.*

Q: What are the **indications** for lobectomy?

A: As follows:

- Localized bronchiectasis (if recurrent haemoptysis or uncontrolled symptoms).
- Malignancy.
- Solitary pulmonary nodule.
- Bronchial adenoma.
- In some case of lung abscess.

Q: What are the **indications** for pneumonectomy?

A: As follows:

- Extensive bronchiectasis involving whole lung.
- Bronchial carcinoma.
- Massive fibrosis with repeated chest infection.
- Massive collapse.

Q: What investigation should be done?

A: Chest x-ray, which shows-

- Rib resection.
- Trachea and apex beat (mediastinum) are shifted.

RHEUMATOID LUNG

Instruction by the examiner:

- Examine the chest. Or, auscultate the back of the chest.

Presentation of a Case:

Inspection:

- The patient is dyspnoeic.
- Respiratory rate is 30/min.

Palpation:

- Trachea is central in position.
- Apical beat is in left fifth intercostal space, just medial to the midclavicular line.
- Chest expansion is reduced symmetrically.
- Vocal fremitus is normal on both side.

Percussion:

- Percussion note is resonant over both lung fields.

Auscultation:

- Breath sound is vesicular with prolonged expiration.
- Bilateral basal end inspiratory fine crepitations are present, unaltered by coughing.
- Vocal resonance is normal.

My differential diagnoses are

- DPLD.
- Bilateral bronchiectasis.

Q: What **relevants** do you like to see in this case?

A: I want to examine the hands to see signs of rheumatoid arthritis, dermatomyositis, skin (systemic sclerosis).

***N.B.:** While examining the back of the chest—keep patient's right hand on the left shoulder and left hand on the right shoulder. Look at both the hands carefully (to see signs of rheumatoid arthritis), a clue for your diagnosis.*

Q: What are the **pulmonary features** of rheumatoid arthritis?

A: As follows:

- Pleurisy.
- Pleural effusion (may be bilateral).
- Fibrosing alveolitis (DPLD).
- Nodules in the lungs (Caplan's syndrome).
- Obliterative bronchiolitis (rare).
- Pulmonary fibrosis.

Q: What is the **commonest** respiratory complication in RA?

A: Pleural involvement, either pleurisy or pleural effusion.

Q: What is Caplan's syndrome?

A: Rheumatoid lung nodules with pneumoconiosis is called Caplan's syndrome. Common in coal-workers' pneumoconiosis, may occur in other pneumoconiosis (e.g., silicosis, asbestosis). Nodules are rounded, may be single or multiple, 0.5 to 2.5 cm, present in the periphery of lung. No treatment is necessary for nodules only. However, these may rupture causing pneumothorax or may cavitate and cause haemoptysis. It may be confused with tuberculosis or neoplasm.

Q: Is there any evidence of bronchial carcinoma in rheumatoid lung disease?

A: Rarely, bronchial carcinoma may occur as a complication, more in smokers, may also occur in non smokers.

ABDOMEN

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ABDOMEN

'The art of medicine consists of amusing the patient while nature cures the disease'
—Voltaire

INTRODUCTION

Disease related to abdomen or examination of abdomen is quite common in any examination. Many short cases or even long cases are also selected. Usually examiner used to ask:

- Examine the abdomen or examine the abdomen and see the relevants.
- Palpate the abdomen. What are your findings?
- Look at the abdomen (in a case of distended abdomen, localized or generalized). What do you think the causes in this case?

Once asked to examine the abdomen, very likely underlying findings are:

- Splenomegaly.
- Hepatomegaly.
- Hepatosplenomegaly.
- Abdominal mass (in epigastrium, right or left iliac fossa, flanks, central or lower abdomen, renal mass bilateral or unilateral, polycystic kidney and transplanted kidney).
- Ascites or ascites with splenomegaly or hepatomegaly.
- Engorged vein in abdomen (also chest).
- Abdominal striae.
- Abdominal aortic aneurysm.
- Normal abdomen.

In most of the cases, there is usually splenomegaly, hepatomegaly, hepatosplenomegaly, abdominal mass or ascites. Keeping these in mind, examine carefully and present the case systematically. At the same time, you must be ready to answer the relevant questions, e.g.:

- Suppose the patient has splenomegaly or hepatomegaly or hepatosplenomegaly. Examiner used to ask, 'What are the **causes**? What **relevant** do you like to see? What **investigations** do you suggest?'
- Suppose the patient has a mass in epigastrium or iliac fossa. Examiner usually asks, 'What do you think the **causes**? What **else** do you want to see? What **investigations** do you suggest?'
- If the abdomen is distended, examiner may ask, 'What are the **causes of abdominal distension**? Do you think the patient has **ascites**? How to **confirm** ascites?'

- There may be engorged veins. Examiner may ask, 'What are the **causes of engorged vein** in abdomen? What **else** do you like to see?' (Flow of blood should be seen).
- If multiple striae are present, examiner may ask, 'What are the **likely causes**?'
- Sometimes the examiner may ask to examine a normal abdomen to see whether you can examine properly in a methodical way.
- Be careful, you must not make finding which is not present. Sometimes a finding may be missed (e.g., small spleen or liver or mass). In such a case, a good examiner may give you a chance, '**examine again**'. In such situations, definitely you have missed some finding like just palpable spleen, small liver or mass etc. So, be more careful in such situations and examine more carefully.

EXAMINATION ROUTINE (ABDOMEN)

Proceed as follows:

- Introduce yourself, ask for permission, 'Good morning, I am Dr. . . . I would like to examine your tummy. Would you please allow me to do so? Please tell me if I hurt you or if you feel any discomfort'.
- Remain on the right side, ensure that the patient is lying flat in a supine position (remove any extra pillow with permission), hands of the patient to be kept by the side. Abdomen is exposed from inframammary region to just above the pubic symphysis (do not expose the genitalia to embarrass the patient).
- Quickly look from head to foot. There may be some clue for the diagnosis. For example, chronic liver disease, Chronic kidney disease (CKD) or other renal diseases (nephrotic syndrome and acute glomerulonephritis). In hereditary haemolytic anaemia, frontal and parietal bossing, mongoloid facies etc.

Inspection:

- Shape of abdomen: may be normal, distended or shrunken (scaphoid). If distended, whether it is generalized or localized (epigastrium, right or left hypochondrium, iliac fossa or central part).
- To see the movement of abdomen, ask the patient to take deep breath in and out, look from either leg or head end to see whether the movement is equal at all sides.
- Visible peristalsis.
- Visible pulsation (in epigastrium).
- Umbilicus (inverted or everted).
- If visible or engorged veins are present, mention the site (central part, flank, below or above umbilicus, around umbilicus), **see the flow** (upwards, downwards or away from the umbilicus).
- If striae are present, mention the site (also, see the colour, size, vertical or horizontal).
- Scar mark (may be surgery or trauma), fistula (Crohn's disease) or stoma (such as colostomy, ileostomy or ileal conduit).
- Pigmentation (may be linea nigra from below umbilicus, erythema ab igne).
- Swelling or mass (mention the site, see whether it is intra-abdominal or extra-abdominal).
- Campbell de Morgan's spot (which are red, nodular lesion, in middle age or elderly).
- Finally, look at the groin to see hernia (ask the patient to cough), pubic hair and genitalia (with permission).

Palpation:

- Ask if there is any pain in the abdomen (examine that part at last).
- Ensure that your hand is warm, put the palm gently rather than tip of fingers, keeping the hand flat on abdominal wall with gentle flexion of metacarpophalangeal joints.
- You should be in horizontal position by kneeling at the patients side, wrist and forearm in the same plane.
- During palpation, look at face to see whether patient **winces** with pain.
- If ascites is present, do not forget to palpate by **dipping** technique.
 1. First, perform superficial palpation, feel for rigidity or any mass. Hard periumbilical lymph node (called **Sister Mary Joseph nodule** is highly suggestive of metastasis from pelvic or gastrointestinal tract primary tumour).
 2. Tenderness.
 3. **Liver:** Start from right iliac fossa, ask the patient, 'turn your face to left side, keep your mouth open, take deep breath in and out'. Press and proceed during inspiration and look at the patient's face.

If liver is **palpable**, see the **following points**:

- Size: Measure in centimetre (with tape from costal margin in right midclavicular line, **not finger** measurement). If left lobe is enlarged, measure from xiphoid process.
- Margin: round or smooth or sharp).
- Surface (smooth or irregular).
- Tenderness.
- Consistency: soft or firm or hard.
- Upper border of liver dullness (by percussion).
- Auscultation over liver for **bruit** or **rub** (often forgotten).

N.B. Pulsatile liver may be present. In such a case, put your left hand on the back, right hand over the liver, press gently and see movement of right hand.

4. **Spleen:** Keep your left hand in lowermost part of left side of chest with slight pressure. Starting from the right iliac fossa, ask the patient, 'turn your face to left side, keep your mouth open, take deep breath in and out'. If it is not felt, turn the patient halfway towards right and palpate again.

If spleen is palpable, see the following points:

- Size: Measure in centimetre along its long axis from costal margin in the anterior axillary line towards right iliac fossa, also from costal margin in left midclavicular line.
- Feel splenic notch.
- See, get above the swelling of spleen (insinuate right index finger between spleen and left costal margin).
- Percuss over spleen and continue up to left lower part of chest (to see the continuation of splenic dullness).
 5. Palpate both right and left kidneys (by ballottement).
 6. Gall bladder.
 7. Any mass (see below).
 8. Feel for para-aortic lymph nodes (by tip of fingers).
 9. Palpate hernial orifice (ask the patient to cough, then see and palpate).
 10. Palpate testis (with permission of patient).
 11. Finally, PR examination (if the examiner asks). **Never done in the examination.**

Percussion:

- Usually a light percussion is done. Note normal tympanic sound.
- See the area of liver dullness and splenic dullness.
- If there is suspicion of ascites, see the shifting dullness.
- Fluid thrill (if tense ascites).

Auscultation:

- Bowel sound: Normal or sluggish or absent (if paralytic ileus).
- Over liver (hepatic bruit or rub).
- Renal bruit (2 cm above the umbilicus and lateral to midline).
- Bruit of aortic aneurysm (if any).
- Splenic rub (rarely found).
- Venous hum (heard between xiphisternum and umbilicus). It is a continuous, low pitch soft murmur. Presence of venous hum indicates portal hypertension (rare finding). It is due to large volume of blood flowing in umbilical or paraumbilical vein in falciparum ligament due to porto-systemic shunt.

N.B.: When venous hum is present with prominent veins in anterior abdominal wall, it is called Cruveilhier–Baumgarten syndrome.

After finishing, ask the examiner for permission, ‘May I see the relevants please?’ or examiner may ask, ‘What relevants do you like to see?’

Relevant findings to be seen according to the findings in abdomen and suspicion of causes:

- If the patient has ascites and splenomegaly which may be due to CLD, your answer will be, ‘I want to see the stigmata of CLD’ (see page 393).
- If the patient has splenomegaly or hepatosplenomegaly, which may be due to lymphoma, leukaemia or CLD, your answer will be, ‘I want to see lymph nodes in other parts of the body, bony tenderness, anaemia or stigmata of CLD’.
- In young or child, if the patient has splenomegaly or hepatosplenomegaly, which may be due to hereditary haemolytic anaemia, your answer will be, ‘I want to see anaemia, jaundice, frontal and parietal bossing in head, prominent malar bones or mongoloid facies, also family history’. If CLD is suspected, examiner may ask, ‘What specific signs do you like to see in a child or young age?’ Your answer will be, ‘I want to see KF ring in eye (found in Wilson’s disease) and emphysema in chest (found in α_1 -antitrypsin deficiency)’.
- If mass in epigastrium due to carcinoma of stomach, your answer will be, ‘I want to see the left supraclavicular lymph node’ (Virchow’s gland).
- If renal mass and the patient looks anaemic, look for arteriovenous fistula in the wrist or below the clavicle (haemodialysis). Also check blood pressure, puffy face and oedema (may be due to CKD).

If any mass is found, look for the following points:

See whether it is intra-abdominal or extra-abdominal. Ask the patient to raise his head and press over the forehead. See and palpate the mass again. If it disappears or less prominent, it

is intra-abdominal. If more prominent, it is likely to be extra-abdominal. Next, see the following points:

- Site.
- Size.
- Shape (round, regular or irregular).
- Surface (smooth or irregular).
- Consistency (soft or firm or hard).
- Tenderness.
- Mobility (mobile or fixed).

N.B.: A fixed mass that does not move with respiration is highly suggestive of retroperitoneal (such as retroperitoneal sarcoma) or colonic mass.

Remember, sometimes the examiner may indicate a particular instruction or give short history and then will ask to examine a particular part. In such case, he will expect specific answers. For example:

- This patient is referred to you from cardiology unit. Palpate the abdomen (in such a case, there may be splenomegaly, which is due to infective endocarditis. Or enlarged and tender liver, which may be due to CCF or chronic constrictive pericarditis. Or ascites due to chronic constrictive pericarditis, even CCF).
- Look at the patient and now palpate the abdomen. The patient may have plethoric face. Splenomegaly indicates polycythaemia rubra vera or bilateral renal mass due to polycystic kidney disease.
- Look at the patient (may have rheumatoid hand) and palpate the abdomen (splenomegaly indicates Felty's syndrome).
- This young lady has thrombocytopenia. Now palpate the abdomen. Presence of splenomegaly is suggestive of SLE.
- This patient has extreme itching. Examine the abdomen (Presence of splenomegaly may be due to polycythaemia rubra vera).
- This middle aged lady has extreme itching. What is the finding in the abdomen? (Presence of hepatomegaly may be due to primary biliary cirrhosis).
- This lady of 21 years is referred from neurology having CVD and right sided hemiplegia. Examine the abdomen (presence of splenomegaly is highly suggestive of SLE with antiphospholipid syndrome).
- This young patient has developed CVD. Examine the heart (there may be mitral stenosis with atrial fibrillation).

READ THE FOLLOWING IMPORTANT FINDINGS ON INSPECTION

If there are **obvious findings on inspection** examiner may ask, 'What do you see? What is this? What are the likely causes?' As for example:

Distended abdomen: Causes of generalized distension (5 F's):

- **Fat** (obesity).
- **Fluid** (ascites).
- **Foetus** (in female of child bearing age).
- **Flatus** (gastrointestinal).
- **Faeces** (constipation).

(Others: Intra-abdominal mass, big ovarian cyst, urinary retention).

Causes of **localized** abdominal distension:

1. Epigastrium (remember the structures in epigastrium):
 - Left lobe of liver (hepatoma, secondaries, liver abscess, hydatid cyst).
 - Pancreas (pancreatic pseudocyst, carcinoma of head of pancreas).
 - Stomach (carcinoma of stomach, lymphoma).
 - Transverse colon (carcinoma of colon)
 - Others: epigastric hernia, aneurysm of aorta (pulsating mass).
2. Right hypochondrium:
 - Hepatic mass (hepatoma, secondaries, liver abscess, polycystic liver, hydatid cyst).
 - Gall bladder (carcinoma, mucocoele, empyema, carcinoma of head of pancreas).
 - Mass in hepatic flexure or right side of transverse colon (carcinoma colon).
3. Left hypochondrium:
 - Splenomegaly (due to any cause).
 - Renal mass and suprarenal mass.
 - Mass in splenic flexure or left side of transverse colon (carcinoma colon).
 - Hydatid cyst.
 - Carcinoma of pancreas (from tail).
4. Hypogastric swelling (below the umbilicus):
 - Bladder (urinary retention).
 - In female (ovarian cyst and pregnancy).
 - Intra-abdominal malignancy.
 - Lymphoma.
 - Tabes mesentericus or mesenteric cyst.
 - Hydatid cyst.



Sister Mary Joseph
nodule



Upper abdominal
swelling



Lower abdominal
distension
(urinary retention)



Scaphoid abdomen

Causes of **scaphoid abdomen** (shrunken):

- Starvation.
- Carcinoma (commonly, oesophagus and stomach).
- Dehydration.

Causes of engorged veins:

1. Superior vena caval obstruction (flow is downwards).
2. Inferior vena caval obstruction (flow is upwards).
3. Portal obstruction (like normal flow) as follows:
 - Veins above umbilicus (flow is upwards).
 - Veins below umbilicus (flow is downwards).
4. In extreme cachexia, engorged veins are present due to loss of subcutaneous fat.
5. Normally present in lean and thin person.

Q: If **engorged vein**, examiner may ask, 'What else would you like to see and why?'

A: I want to see the flow of blood to find out causes (see above).

Q: What is the **normal blood flow** of veins?

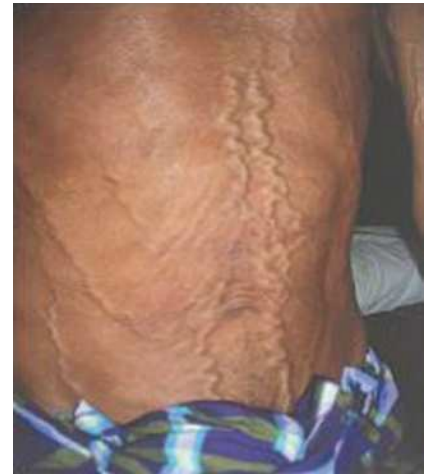
A: As follows:

- Veins above umbilicus (flow is upwards).
- Veins below umbilicus (flow is downwards).

Q: How to **differentiate** between SVC obstruction, IVC obstruction and portal obstruction?

A: As follows:

Points	SVC Obstruction	IVC Obstruction	Portal Obstruction
1. Veins	Usually in the upper abdomen and chest wall	Mostly in the flanks and rarely in the lower abdomen	In the upper and in the lower abdomen, also around the umbilicus (caput medusae)
2. Flow	Downwards	Upwards	Away from the umbilicus (flow of veins upwards above the umbilicus and downwards below it)



Engorged veins

N.B. There will be other signs of SVC, IVC or portal vein obstruction.

Q: What are the **signs of SVC obstruction**?

A: As follows:

- Face is plethoric or reddish, oedematous or puffy, suffused.
- Eyes with conjunctival suffusion, chemosis and periorbital oedema.
- Neck veins are engorged and non-pulsatile.

Q: What are the **signs of IVC obstruction**?

A: As follows:

- Lower limbs: Swollen and oedematous with engorged veins.
- Buttock and groin are also swollen and oedematous.

N.B. In IVC obstruction, engorged veins are due to dilated anastomotic channel between superficial epigastric and circumflex iliac veins below and lateral thoracic veins above, conveying blood from long saphenous vein to axillary vein.

Q: What are the signs of portal obstruction?**A:** As follows:

- Splenomegaly (single most definitive sign).
- Ascites.
- Oesophageal varices by endoscopy and also haemorrhoid by proctoscopy.

Q: What is caput medusae?

A: Caput medusae refer to dilated veins radiating from the umbilicus, found in portal obstruction. It is named after its resemblance to the Greek goddess *Medusae*, whose head was adorned with snakes that radiated from her head (*Caput* means head). It is a rare finding.

Q: What is striae? What are the causes?

A: These are wrinkled, linear, white or pink coloured marks over the skin. Striae are due to stretching of skin causing rupture of elastic fibres. Causes of striae are:

- Striae gravidarum (white or pink, narrow lines, in abdominal wall due to pregnancy, below the umbilicus).
- Obesity (whitish narrow lines, usually longitudinal, <2 mm).
- Cushing's syndrome (wide lines, pink or purple or red, mostly horizontal or oblique. Pink or red colour is due to increased vascularity.)
- Ascites.

Q: What is Grey Turner's sign?

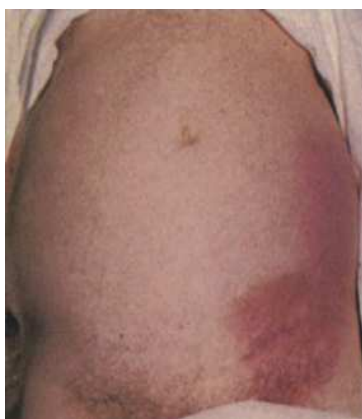
A: It is the skin discolouration in the flanks of abdominal wall due to extraperitoneal bleeding (haemoperitoneum due to any cause).

Q: What is Cullen's sign?

A: It is the skin discolouration around the umbilicus, usually a faint bluish hue. It is due to haemoperitoneum.



Striae gravidarum



Grey Turner's sign



Cullen's sign

Causes of visible epigastric pulsation:

- Normally, in thin body build.
- Right ventricular hypertrophy.
- Aneurysm of the aorta.
- Pulsatile liver.
- Mass overlying the abdominal aorta (e.g., carcinoma stomach).

Causes of eversion of umbilicus:

- Ascites (slit is transverse).
- Ovarian cyst (slit is vertical).
- Umbilical hernia.

Causes of multiple fistula in abdomen:

- Crohn's disease.
- Abdominal tuberculosis.
- Actinomycosis.
- Trauma.

Causes of haemoperitoneum:

- Rupture of spleen.
- Rupture of ectopic pregnancy.
- Acute haemorrhagic pancreatitis.
- Any cause of bleeding (blood dyscrasia and excess anticoagulant therapy).

Multiple small, firm skin nodules in the anterior abdominal wall may be due to:

- Neurofibroma.
- Disseminated malignancy (secondaries).
- Sarcoidosis.
- Lipoma.

Q: What is Sister Mary Joseph nodule?

A: Sister Mary Joseph nodule or more commonly node, also called Sister Mary Joseph sign, is a palpable nodule bulging into the umbilicus as a result of metastasis of a malignant cancer in the pelvis or GIT. Primary sources may be from the following:

- Gastrointestinal malignancies (Carcinoma of stomach, colon or pancreatic cancer, mostly of the tail and body of the pancreas), more in male.
- Pelvic or gynaecological cancers account for about 1 in 4 cases (primarily ovarian cancer, uterine cancer).
- Rarely from Pseudomyxoma peritonei, unknown primary tumours, urinary or respiratory tract malignancies cause umbilical metastases.

How the metastases reach the umbilicus is unknown. Probable mechanisms are direct transperitoneal, lymphatics, haematogenous spread or via remnant structures such as the falciform ligament, median umbilical ligament or remnant of the vitelline duct. Sister Mary Joseph nodule is associated with multiple peritoneal metastases and a poor prognosis.

Q: What is Riedel's lobe?

A: It is a tongue-like projection from inferior surface of right lobe of liver, felt in right hypochondrium. It is a normal finding, common in women, rarely may be very large up to the right iliac fossa. It may be confused with enlarged gall bladder or enlarged right kidney.

SPLENOMEGALY (NOT HEPATOMEGALY)

Instruction by the examiner:

- Examine the abdomen or examine the abdomen and see the relevants.
- Palpate the abdomen. What are your findings?

Presentation of a Case:

- Spleen is enlarged, . . . cm from left costal margin, in the anterior axillary line towards right iliac fossa, also . . . cm from costal margin in left midclavicular line.
- Soft or hard or firm in consistency (mention accordingly).
- Splenic notch is present.
- Finger cannot be insinuated between the spleen and left costal margin.
- On percussion, there is dullness over spleen, which is continuous up to left lower part of chest.

Q: Why it is spleen, not kidney?

A: It is spleen because:

- The mass is in left hypochondrium.
- Moves with respiration downward and towards the right iliac fossa.
- I could not get above the swelling and finger could not be insinuated between the mass and left lower rib.
- There is splenic notch (definitive sign).
- Percussion note is dull over the mass and continuous up to the left lower part of chest.

Differences between spleen and kidney:

Spleen	Kidney
1. It is in the left hypochondrium.	1. It is in the lumbar region or loin.
2. Moves with respiration towards right iliac fossa.	2. Moves downward and forward.
3. Well defined medial border.	3. Round in shape.
4. Notch is present.	4. Absent.
5. Get above the swelling: Absent and finger cannot be insinuated between the mass and left costal margin.	5. Present and finger can be insinuated between the mass and left costal margin.
6. On percussion: dullness over the mass, which is continuous with the left lower chest.	6. Colonic resonance over the mass.
7. Palpable.	7. Ballotable.

N.B. Remember the following points:

- Spleen must be enlarged at least 2 to 3 times before it can be felt. Once a spleen is palpable, it is definitely enlarged (always pathological).
- Enlarged spleen may be: Mild <4 cm, moderate 4 to 8 cm or huge >8 cm.
- Spleen lies beneath 9th, 10th and 11th rib. Long axis of spleen lies along the 10th rib.
- It enlarges towards the right iliac fossa. In children, may be enlarged towards the left iliac fossa.
- If kidney is hugely enlarged, colonic resonance may be absent, get above the swelling may not be possible.

Q: What are the causes of mass in left hypochondrium (D/D of splenomegaly)?

A: As follows:

- Splenomegaly.
- Enlarged left kidney.
- Carcinoma colon (left hepatic flexure).
- Carcinoma of stomach (greater curvature).
- Carcinoma tail of pancreas.
- Omental mass.

Q: Mention one single investigation.

A: USG of whole abdomen.

Q: What **relevants do you want to see in a case of splenomegaly?**

A: As follows:

- Lymph nodes (may be found in lymphoma, leukaemia, SLE, viral infection, sarcoidosis).
- In early age: anaemia, jaundice. Also frontal, parietal bossing and mongoloid facies (found in hereditary haemolytic anaemia).
- Signs or stigmata of CLD (see page 393).
- Heart to see murmur (SBE).
- Bony tenderness (in leukaemia).
- Pigmentation (in kala-azar).

Q: What are the **causes of splenomegaly?**

A: Mention the causes according to the age of the patient:

If Middle Aged or Elderly, the Causes are:	If Young or of Early Age, the Causes are:
• Malaria. • Kala-azar. • Chronic myeloid leukaemia. • Myelofibrosis. • Lymphoma. • Cirrhosis of liver with portal hypertension. • Chronic lymphatic leukaemia. • Tropical splenomegaly syndrome.	• Malaria. • Kala-azar. • Hereditary haemolytic anaemia (β-thalassaemia major, HbE disease, E β-thalassaemia and hereditary spherocytosis). • Lymphoma. • Cirrhosis of liver with portal hypertension (causes of which are Wilson's disease and α_1-antitrypsin deficiency).

Causes of huge splenomegaly (may cross the midline):

- Chronic kala-azar.
- Chronic malaria.
- CML.
- Myelofibrosis.
- Cirrhosis of liver with portal hypertension (occasionally, common in early age).
- Hairy cell leukaemia.
- Adult Gaucher's disease.
- Rapidly progressive lymphoma.

Causes of just palpable spleen (spleen tip):

- Enteric fever.
- Subacute bacterial endocarditis (SBE).
- Viral infection (infectious mononucleosis and CMV infection).
- Collagen disease (SLE).
- Sarcoidosis.
- Polycythaemia rubra Vera.
- All causes of huge splenomegaly in the early stage.

Causes of lymphadenopathy with splenomegaly:

- Lymphoma.
- Leukaemia (acute lymphoblastic leukaemia, chronic lymphocytic leukaemia).
- Viral infection (infectious mononucleosis, CMV infection and HIV).
- Collagen disease (SLE).
- Kala-azar (African kala-azar, also Chinese kala-azar).
- Others (sarcoidosis, brucellosis, toxoplasmosis, disseminated TB).

Causes of fever with splenomegaly:

- Enteric fever.
- Malaria.
- Kala-azar.
- SBE.
- Viral infection (infectious mononucleosis and CMV infection).
- Lymphoma.
- Leukaemia.
- Collagen disease (SLE).
- Brucellosis.
- Toxoplasmosis.
- Disseminated TB.

Causes of splenomegaly with ascites:

- Cirrhosis of liver with portal hypertension.
- Collagen disease (SLE).
- Lymphoma.
- Leukaemia.
- Disseminated TB.

Q: How **consistency** of spleen may help in diagnosis of splenomegaly?

A: It shows the following:

1. If the **spleen is soft**, causes may be:
 - Enteric fever.
 - SBE.
 - Viral infection.
 - Acute leukaemia.
2. If the **spleen is firm**, causes may be:
 - Cirrhosis of liver with portal hypertension.
 - CML.

3. If the **spleen is hard**, causes may be:

- Malaria.
- Kala-azar.

Q: What are the causes of splenic atrophy or hyposplenism?

A: As follows:

- Sickle cell disease (auto-splenectomy due to repeated infarction in 2nd decade about 16 years of age).
- Coeliac disease.
- Dermatitis herpetiformis.
- Occasionally in inflammatory bowel disease (ulcerative colitis).
- Essential thrombocythaemia.

Q: What are the risks of hyposplenism or splenectomy?

A: After splenectomy:

- Increased risk of pneumococcal infection (pneumococcal vaccine should be given, 2 to 3 weeks before splenectomy).
- Meningococcal and *Haemophilus* infection.
- Malaria.

Q: What is the blood picture after splenectomy?

A: Blood pictures after splenectomy or hyposplenism:

- RBC shows Howell–Jolly body (nuclear remnants in RBC), target cell, acanthocytic cells (crenated or irregular RBC) and increased reticulocyte.
- WBC: Initially neutrophilic leucocytosis. Normal after few weeks. Later, high lymphocytes and monocytes.
- Platelet: high immediately, normal in 1 to 2 months. In some cases, thrombocytosis may persist.

Q: What are the indications of splenectomy?

A: As follows:

- Hereditary spherocytosis.
- ITP (when there is failure of drugs).
- Autoimmune haemolytic anaemia (when there is failure of drugs).
- Huge splenomegaly with pressure symptoms.
- Hairy cell leukaemia.
- Rupture of spleen.
- Hypersplenism (suggested by repeated requirement of blood transfusion in a short interval).

Q: What is hypersplenism? What are the causes?

A: It is a syndrome characterized by:

- Splenomegaly.
- Reduction of one or more blood cells (pancytopenia).
- Increase cellularity of bone marrow.
- Improvement of blood picture after splenectomy.

Any cause of splenomegaly may cause hypersplenism, commonly found in:

- Haematological disease.
- Portal hypertension.
- Felty's syndrome.
- Lymphoma.

SPLENOMEGALY (TROPICAL SPLENOMEGALY SYNDROME)

Instruction by the examiner:

- Examine the abdomen or examine the abdomen and see the relevants.
- Palpate the abdomen. What are your findings?

Presentation of a Case:

- Present the cases as described in splenomegaly.

Mention tropical splenomegaly syndrome (TSS) as a cause of splenomegaly lastly, if asked.

Q: What is tropical splenomegaly syndrome?

A: In hyperendemic malarial area, there is gross splenomegaly associated with exaggerated immune response to repeated malarial infection, called tropical splenomegaly syndrome (also called hyper-reactive malarial splenomegaly. Previously it was called Banti's syndrome). It is characterized by anaemia, massive splenomegaly and high IgM levels. Malarial parasites are scanty or absent.

Causes: Aberrant immunological response to repeated infection by any species of malarial parasite. There is increased production of cytotoxic IgM antibody to CD8+ T lymphocytes, CD5+ T lymphocytes and increased ratio of CD4+ T cells: CD8+ T cells. In African patient, there is increase in B lymphocytes, confuses with chronic lymphatic leukaemia.

Other features of TSS:

- Common in older children and adults. Splenomegaly is common, hepatomegaly is also common.
- There may be anaemia, pancytopenia and evidence of hypersplenism.
- Acute haemolytic episode may occur and portal hypertension may also occur.

Cause of death: Due to infection. Respiratory and skin infections are common.

Q: How to diagnose TSS?

A: As follows, according to the following criteria:

Major criteria:

- Gross splenomegaly: 10 cm or more in adult for which no other cause can be found.
- High serum IgM >2 standard deviations or more above the local mean.
- Clinical and immunologic responses to antimalarial therapy.
- Regression of splenomegaly by 40% by 6 months after start of therapy.
- High antibody levels of *Plasmodium* species ($\geq 1:800$).

Minor criteria:

- Liver biopsy shows sinusoidal lymphocytosis, hyperplasia and aggregates of IgM in Kupffer cells (detected by immunofluorescence).
- Lymphocytic proliferation.
- Hypersplenism.
- Normal cellular and humoral responses to antigenic challenge excluding plasmodium.
- Familial occurrence.

Diagnosis is done by exclusion of other cause of splenomegaly. Common investigations are:

- CBC (which shows anaemia, thrombocytopenia and lymphocytosis).
- Bone marrow study shows lymphocytes infiltration.
- Liver biopsy shows Kupffer cells hyperplasia, lymphocytes infiltration and round-cell infiltration in portal tract. In some cases, fibrosis leading to portal hypertension.

Treatment:

1. In endemic area, chemoprophylaxis should be taken:
 - Proguanil 100 mg/day **plus** chloroquine 600 mg weekly.
 - Folic acid 5 mg/day.
2. In non-endemic area:
 - Treatment of malaria: short course (with chloroquine). Patients who continue to be exposed to malaria-endemic regions require intermittent therapy or possibly lifelong treatment.
 - Splenomegaly and anaemia usually resolve over a period of months with treatment.
 - In some cases refractory to therapy, clonal lymphoproliferation may develop and can then evolve into a malignant lymphoproliferative disorder.

HEPATOSPLENOMEGALY

Instruction by the examiner:

- Examine or palpate the abdomen and see the relevants.

N.B.: Proceed in the form of inspection, palpation, percussion and auscultation. Only positive findings are described.

Presentation of a Case:

- The abdomen is distended, generalized or in right or left hypochondrium (mention accordingly).

The liver is (mention your findings):

- Enlarged, . . . cm from right costal margin in midclavicular line.
- Margin is sharp (or round).
- Surface is smooth (or irregular, nodular, single or multiple).
- Consistency is firm (or soft or hard).
- Tender (or non-tender).
- Upper border of the liver dullness is in right . . . intercostal space, in midclavicular line.
- There is no (or yes) hepatic bruit or rub.

The spleen is (mention your findings):

- Enlarged . . . cm from left costal margin, in left anterior axillary line (towards right iliac fossa), also . . . cm from costal margin in left midclavicular line.
- Soft or hard or firm in consistency (mention accordingly).
- Splenic notch is present.
- Finger cannot be insinuated between spleen and left costal margin.
- On percussion, dullness over spleen, which is continuous up to left lower part of chest.

My diagnosis is **Hepato-splenomegaly**.

Q: What do you think the **causes** of hepato-splenomegaly in this case?

A: Mention the causes of that patient according to the age:

If the patient is **middle-aged or elderly**, causes are:

- Kala-azar.
- Malaria.
- Chronic myeloid leukaemia.
- Myelofibrosis.
- Lymphoma.
- CLD with portal hypertension.

If the patient is **young or early age**, causes are:

- Kala-azar.
- Malaria.
- Hereditary haemolytic anaemia (β -thalassaemia major, HbE disease, HbE β -thalassaemia, hereditary spherocytosis).
- Lymphoma.
- CLD with portal hypertension.

Q: What else or relevants do you want to see?

A: I want to see:

- Pigmentation (in kala-azar, also CLD and haemochromatosis).
- Lymph nodes (in lymphoma, CLL, also in viral infection).
- Signs or stigmata of CLD (page 393).
- Bony tenderness (in CML).
- In young or child: anaemia, jaundice, frontal and parietal bossing, mongoloid facies (which are found in hereditary haemolytic anaemia).

Q: What history do you like to take?

A: As follows:

- History of fever (may be due to malaria, kala-azar, lymphoma, CML). If fever is present, details history should be taken such as type of fever (continuous, remittent, intermittent etc.), associated chill and rigor, travel to endemic zone, history of resident zone.
- Previous history of jaundice and liver disease (in CLD).
- In child or early age, there may be history of growth retardation, anaemia, jaundice, family history in hereditary haemolytic anaemia.

Q: Mention one simple investigation that may help to diagnose or exclude some diseases.

A: CBC with PBF examination. By this, I can diagnose:

- Malaria.
- Kala-azar (CBC shows leucopenia, lymphocytosis and monocytosis. If blood count is repeated after some days, it shows progressive leucopenia. Rarely LD body may be found in buffy coat).
- Leukaemia (CML).
- Myelofibrosis (it shows pancytopenia, leucoerythroblastic blood picture, tear or pear-drop poikilocyte).
- Hereditary haemolytic anaemia (it shows microcytic hypochromic blood picture).
- Multiple myeloma (it shows high ESR and rouleaux formation).

Q: What investigations do you suggest in hepato-splenomegaly?

A: As follows:

1. Routine investigations:
 - CBC, platelet, PBF and malarial parasite (see the findings as described above).
 - Chest X-ray (in lymphoma and leukaemia, shows bilateral hilar lymphadenopathy).
 - Ultrasonogram of whole abdomen (may be lymphadenopathy, change in liver in CLD).
2. Others according to the suspicion of cause:
 - If CLD is suspected: investigate accordingly (see page 393).
 - If hereditary haemolytic anaemia is suspected: Hb electrophoresis and X-ray of skull, hands.
 - If kala-azar is suspected: investigate accordingly (see page 357).
 - If lymphoma is suspected: Chest X-ray (shows bilateral hilar lymphadenopathy), FNAC or biopsy of lymph node.
 - If CML or myelofibrosis is suspected: bone marrow study.

Q: What are the causes of **lymphadenopathy with hepatosplenomegaly**?

A: As follows:

- Lymphoma.
- Chronic lymphatic leukaemia (may be found in CML with blastic crisis).
- Acute lymphatic leukaemia.
- SLE.
- Disseminated TB.
- Others: infectious mononucleosis, CMV infection, HIV, kala-azar (in Chinese and African kala-azar), sarcoidosis, brucellosis and toxoplasmosis.

Q: What are the **causes** of **hepatosplenomegaly**?

A: As follows:

1. Infection:
 - Kala-azar.
 - Malaria.
 - Schistosomiasis (in Middle East and Africa).
 - Enteric fever.
 - Viral infections such as infectious mononucleosis and cytomegalovirus infection.
2. Myeloproliferative diseases:
 - CML.
 - Polycythaemia rubra vera.
 - Myelofibrosis.
 - Essential thrombocythaemia.
3. Lymphoproliferative diseases:
 - Chronic lymphatic leukaemia (CLL).
 - Multiple myeloma.
 - Waldenström macroglobulinaemia.
 - Lymphoma.
4. Cirrhosis of liver with portal hypertension (In these 3 types, liver is enlarged. In other types of cirrhosis, no hepatomegaly):
 - Primary biliary cirrhosis,
 - Haemochromatosis,
 - Alcoholic cirrhosis
5. Collagen diseases (SLE, Sjögren's syndrome, Felty's syndrome).
6. Others:
 - Sarcoidosis.
 - Amyloidosis.
 - Thyrotoxicosis (in Graves disease, rare).
 - Acromegaly.
 - Storage disease (Gaucher's disease and glycogen-storage disease).
 - Polycystic disease.

Q: What are the causes of **fever with hepatosplenomegaly**?

A: As follows:

- Malaria.
- Kala-azar.
- Enteric fever.
- Viral infection (infectious mononucleosis and CMV infection).
- Lymphoma.
- Leukaemia (CGL, CLL, ALL, AML).
- Collagen disease (SLE).
- Disseminated TB.
- Brucellosis.
- Toxoplasmosis.
- Sarcoidosis.

HEPATOSPLENOMEGALY (DISCUSSION ABOUT MALARIA)

Instruction by the examiner:

- Examine or palpate the abdomen and see the relevants.

Presentation of a case:

Present as described in hepatosplenomegaly.

Malaria is caused by one of four species: *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*. Occasionally, other species found in primates (e.g., *P. knowlesi*) can affect humans.

Mode of transmission: Malaria is transmitted to human by the bite of infected female anopheles mosquitoes. Rarely, it can also be transmitted by blood transfusion, transplacental transmission. 2 life cycles:

- Asexual: in human.
- Sexual: in mosquito.

Q: What **investigations** are done to diagnose malaria?

A: As follows:

- Blood film (both thick and thin).
- Rapid diagnostic test (ICT for falciparum).
- QBC for malaria (fluorescence microscopy based test).

Q: Why **thick** and **thin** films are done?

A: As follows:

- **Thick film:** erythrocytes are lysed, releasing all blood stages of parasite. It is helpful to detect parasite even with low parasitaemia.
- **Thin film:** to detect the species and to quantify the parasite load in *Plasmodium falciparum*.

N.B. Remember the following points:

- *In falciparum malaria: only gametocytes and ring forms are found.*
- *Other species (P. vivax, P. malariae and P. ovale): All stages of erythrocytic cycle such as ring, trophozoite, schizont and gametocyte are found.*
- *Gametocytes are found after about 2 weeks.*
- *Malarial parasites may be found both during febrile and afebrile period. But falciparum is difficult to be found in afebrile period.*
- *Thick film is usually stained by Giemsa, thin film by Giemsa or Leishman.*

Q: What are the species having **exoerythrocytic cycle** (hepatic)? How to treat?

A: As follows:

- **Exoerythrocytic cycle** is present in *P. vivax* and *P. ovale*, persists in liver cell as dormant form called hypnozoite, develop into merozoite months or years later causing relapse of malaria.
- So, after treatment of malaria, primaquine 15 mg daily for 14 days should be given to eradicate exoerythrocytic cycle.
- There is no exoerythrocytic cycle in *P. falciparum* and *P. malariae*, but recrudescence of fever may occur from multiplication of parasite in red cells, which are not eliminated by treatment and immune process.

Q: What is radical cure?

A: Eradication of hypnozoite of vivax and ovale parasite from the liver. It is done by giving primaquine 15 mg daily for 14 days.

Q: What measures should be taken before giving primaquine?

A: Primaquine can cause haemolysis in G6PD deficiency. So, G6PD should be measured before giving primaquine. However, if G6PD is present, primaquine 30 mg weekly for 8 weeks may be given. Primaquine can cause cyanosis due to formation of methaemoglobin in red cells (not dangerous).

Q: What are the common side effects of primaquine therapy?

A: Haemolysis in G6PD deficiency, also chemical cyanosis due to formation of methaemoglobin in red cells.

Q: Which red cells are involved by different species of malaria?

A: As follows:

- *Falciparum* involves red cells of all ages. Hence, haemolysis is severe.
- *Vivax* and *ovale* involve mainly reticulocyte. Hence, haemolysis is less severe.
- *Malariae* involves normoblast, can cause glomerulonephritis and nephrotic syndrome in children.

Q: Why anaemia occurs in malaria?

A: Anaemia is due to:

- Haemolysis of infected and uninfected red cells.
- Dyserythropoiesis.
- Splenomegaly (causing sequestration and haemodilution).
- Reduction of folate store.

Q: What is malignant malaria and benign malaria?

A: As follows:

- **Malignant malaria:** It is due to *P. falciparum*, associated with widespread organ damage due to capillary blockage. It is more serious.
- **Benign malaria:** It is mainly due to *P. vivax*, less frequently by *P. ovale* and *P. malariae*. It is usually less serious.

Q: What are the types of malaria?

A: 3 types:

1. Benign tertian: It is due to *P. vivax* and *P. ovale*, usually mild (*P. vivax* can occasionally cause severe disease).
2. Benign quartan: It is due to *P. malariae*.
3. Malignant tertian: It is due to *P. falciparum*.

Q: What are the **clinical features** of different types of malaria?

A: As follows:

- 1. Benign tertian:** In this type, classical bouts off ever occur on alternate days. The cycle is repeated every 48 hours. Spleen is enlarged (usually in 2nd week) and also liver is enlarged, may become tender. Anaemia develops slowly. Hypnozoites in the liver can cause relapses in the first 2 years after leaving the malarious area.
- 2. Benign quartan:** Usually associated with mild symptoms and bouts of fever every 3rd day. Parasitaemia may persist for many years, with occasional recrudescence of fever or without producing any symptoms. Scanty urine, albuminuria and haematuria may occur. Chronic *P. malariae* infection can cause glomerulonephritis and nephrotic syndrome in children.
- 3. Malignant tertian:** Onset is often insidious, with malaise, headache and vomiting. Cough and mild diarrhoea may occur. No typical paroxysm of fever. It may be continuous, remittent or irregular. Jaundice is common due to haemolysis and hepatic dysfunction. Liver and spleen enlarge, may be tender. Anaemia develops rapidly, also thrombocytopenia. Serious complications may occur.

Cerebral malaria is manifested by confusion, seizures or coma, usually without localizing signs. Children die rapidly without any symptoms other than fever. Abortion and intrauterine growth retardation from parasitization of the maternal side of the placenta are frequent. After splenectomy, there is risk of severe malaria.

Q: What are the **typical features** of fever in malaria?

A: Febrile paroxysm consists of 3 stages:

- 1. Cold stage:** In this stage, the patient feels intense cold with chills and rigor, shivers vigorously, prefers to be covered with warm clothes and blanket. Temperature rises rapidly up to 104°F or more. Pulse is rapid, thready. This stage lasts for 15 to 60 minutes.
- 2. Hot stage:** It follows cold stage. The patient feels intense heat, temperature persists, skin is hot and dry, throws away blanket and clothes. Pulse is full, bounding. Respiration is rapid. Headache, thirst, nausea, vomiting may be present. This stage lasts for 2 to 6 hours.
- 3. Stage of sweating:** After hot stage, fever subsides with profuse sweating. The patient feels comfortable. This stage lasts for 2 to 4 hours.

Q: Which disease or haemoglobinopathy **protects** against malaria?

A: As follows:

- *Falciparum* does not grow well in RBC containing haemoglobin F, C or S. Sickle-cell disease protects against falciparum malaria.
- *Vivax* cannot enter RBC that lacks Duffy blood group (West African and American blacks are protected).

Q: What are the features of severe *P. falciparum* infection?

A: It is defined as 'one or more of the following in the absence of an identified cause and in the presence of *P. falciparum* asexual parasitaemia'. It may involve any systems in the body, causing serious complications and death.

- CNS: Impaired consciousness (cerebral malaria is manifested by confusion, convulsions, diminished consciousness and coma without localizing sign).
- Prostration (generalized weakness).
- Multiple convulsion (>2 episodes in 24 hours).
- Acidosis (plasma HCO_3^- <15 mmol/L or, plasma lactate >5 mmol/L. In severe acidosis, there is deep, rapid, laboured breathing).
- Plasma glucose level of <2.2 mmol/L (<40 mg/dL).
- Severe anaemia, haemoglobin <5 g/dL. Haematocrit <15% in children. In adults, haemoglobin <7 g/dL, haematocrit <20%, parasite count >10,000/microL.
- Renal: S. creatinine >3 mg/dl or blood urea >20 mmol/L (there may be haemoglobinuria in blackwater fever, oliguria, acute renal failure, acute tubular necrosis).
- Jaundice: S. bilirubin >50 micromol/L (3 mg/dL) with parasite count >100,000/ microL.
- Pulmonary oedema: radiologic evidence, O_2 sat <92%, respiratory rate >30/min.
- Significant bleeding: recurrent or prolonged bleeding from nose, gum or venepuncture sites, haematemesis, melaena, DIC.
- Shock.
- Hyperparasitaemia (>10%).

Q: How to treat malaria?

A: As follows:

General treatment:

- Blood transfusion for severe anaemia.
- Monitoring and management of water and electrolyte balance,
- Assessment and treatment of renal and hepatic failure.
- Quinine may cause hypoglycaemia. So monitoring of blood glucose is essential.
- Exchange transfusion may be helpful with persisting high parasitaemia (>10% circulating erythrocyte).
- If coma persists, lumbar puncture and CSF study to exclude meningitis or encephalitis.

Treatment for *P. vivax*, *P. ovale* and *P. malariae* (non-falciparum):

- Chloroquine (150 mg base):
 - 4 tabs on 1st day,
 - 4 tabs on 2nd day,
 - 2 tabs on 3rd day (24 hours apart).
- Or, another regime:
 - 1st day: 4 tablets stat, 2 tablets after 6 hours.
 - From next day: 1 tablet twice daily for 2 to 3 days.
- Then, for radical cure: Primaquine 15 mg daily for 14 days (0.25 to 0.5 mg/kg/day).

Or, (if known resistance to chloroquine, or dual infection with *P. falciparum*):

- Artemisinin-based combination therapy (except artesunate + sulphadoxine-pyrimethamine) for 3 days.
- Then, for radical cure: Primaquine 15 mg daily for 14 days (0.25 to 0.5 mg/kg/day for 2 to 3 weeks).

Treatment for falciparum malaria: Many cases are resistant to chloroquine.**1. Mild or uncomplicated case:**

- Co-artemether (artemether plus lumefantrine):
 - 1st day: 4 tablets stat then 4 tablets after 8 hours,
 - From next day: 4 tablets 12 hourly for 2 days (total 24 tablets).
 - After this, Primaquine (0.75 mg/kg/day) single dose.
- Or, other ACT (see below) for 3 days plus Primaquine (0.75 mg/kg/day) single dose.
- Or, quinine 600 mg (10 mg/kg) 8 hourly for 7 days orally plus doxycycline 100 mg 12 hourly for 7 days plus primaquine (0.75 mg/kg/day) single dose. Dose can be given 12 hourly, if quinine toxicity develops.
- Some quinine resistance is found. So after quinine, doxycycline 100 mg twice daily for 7 days or clindamycin 600 mg 12 hourly for 7 days.
- Or, Artesunate 200 mg daily for 3 days and mefloquine 1 g on day 2 and 500 mg on day 3 may be used.
- Or single dose of sulphadoxine 1.5 g plus pyrimethamine 75 mg (Fansidar 3 tablets).

2. Complicated or severe falciparum infection or cerebral malaria:

- Injection artesunate: 2.4 mg/kg IV at 0, 12 and 24 h, then once daily for 7 days is the treatment of choice. IV should be replaced by oral therapy (2 mg/kg once daily), when the patient can swallow. Total dose is 17 to 18 mg/kg (avoid in pregnancy, unless strongly indicated).
- Or, Artemether may be given in the following dose: 80 mg IM twice daily on 1st day, followed by 80 mg daily for 4 days or 80 mg IM twice daily for 3 days.
- Or, quinine IV initially 20 mg/kg (maximum 1.4 g), with 500 cc 5% dextrose in aqua over 4 hours, then 10 mg/kg 8 hourly (maximum 700 mg per dose) for 7 days, until patient can take orally. The loading dose should not be given if the patient has received quinine, quinidine or mefloquine in previous 24 hours.
- Pre-referral treatment: In remote places with less facilities—
 - Rectal artesunate 10 mg/kg body weight single dose
 - Or, IM quinine, diluted in normal saline, 20 mg/kg body weight divided in two (2) anterior thigh.

Q: What are the ACT (artemisinin-based combination therapy) used in malaria?

A: As follows:

1. Fixed-dose combinations:	
• Artemether–lumefantrine	4 tablets twice daily for 3 days
• Artesunate–amodiaquine	4 mg/kg per day artesunate for 3 days
• Dihydroartemisinin–piperaquine	4 mg/kg per day dihydroartemisinin for 3 days
2. Fixed-dose, co-packaged, separate tablets	
• Artesunate–mefloquine	4 mg/kg per day artesunate for 3 days
• Artesunate–sulphadoxine–pyrimethamine	4 mg/kg per day artesunate for 3 days
3. Alternatives where no combination packages are available	
• Artesunate + clindamycin	2 mg/kg per day + 10 mg/kg twice daily for 7 days
• Artesunate + doxycycline	2 mg/kg per day + 3.5 mg/kg per day for 7 days

Q: How to prevent malaria in travellers (called chemoprophylaxis)?**A:** As follows:

1. No chloroquine resistance:
 - Chloroquine 300 mg base weekly or proguanil 200 mg daily. Should be started 1 week before and continued 4 weeks after travel.
2. Limited chloroquine resistance:
 - Chloroquine 300 mg base weekly and proguanil 200 mg daily. Both should be started 1 week before and continued 4 weeks after travel.
 - Or, doxycycline 100 mg daily. Should be started 1 week before and continued until 4 weeks after travel.
 - Or, malarone (atovaquone–proguanil) 1 tablet daily, from 1 to 2 days before travel until 1 week after return.
 - Or, mefloquine 250 mg weekly. Should be started 2 to 3 weeks before travel and continued until 4 weeks after.
3. High chloroquine resistance:
 - Mefloquine 250 mg weekly. Should be started 2 to 3 weeks before travel and continued until 4 weeks after.
 - Or, doxycycline 100 mg daily. Should be started 1 week before and continued until 4 weeks after travel.
 - Or, malarone (atovaquone–proguanil) 1 tablet daily. Should be started 1 to 2 days before travel until 1 week after return.

Q: What are the complications of malaria in pregnancy?**A:** As follows:

- Foetal complications: Still birth, low birth weight, foetal distress. High foetal death in falciparum malaria, especially in the last trimester. Congenital malaria may occur in 5% cases.
- Maternal complications: Maternal death, abortion, premature labour, anaemia, hypoglycaemia, acute pulmonary oedema.

Q: How to treat malaria in pregnancy?**A:** As follows:**In *P. vivax* and *P. ovale* infection:**

- Chloroquine may be given as usual dose.
- If no response to chloroquine, quinine 600 mg 8 hourly for 1 week.
- For radical cure: In *P. vivax* and *P. ovale* infection, no primaquine during pregnancy and lactation. So, chloroquine 600 mg weekly should be given, continued until delivery and breast-feeding are completed. Then, G6PD should be measured. If it is normal, primaquine is given to prevent relapse.

In *P. falciparum* malaria:

1. Uncomplicated—
 - 1st trimester—quinine plus clindamycin, or quinine 600 mg 8 hourly for 1 week. Or, ACT or artesunate plus clindamycin may be given (though safety of ACT is not assuring).
 - 2nd and 3rd trimester—Artemether + lumefantrine or Dihydroartemisinin + piperaquine or Mefloquine + artemisinin derivative may be given.
2. In severe malaria—I.V. artesunate. If not available, IM artemether or, IV quinine (until artesunate is obtained).

Q: What is pernicious malaria? What are the causes, clinical features and treatment?

A: It is a severe form of falciparum malaria in which there is widespread capillary blockage by the parasitized RBC causing multiple organ damage. If not treated, the patient may die within 1 to 3 days. It occurs when >5% of RBC are parasitized.

Pathogenesis: Parasitized RBC develops knob-like projections on the surface, becomes sticky and adheres to the endothelium of capillaries of different organs. As a result, there is blockage with severe anoxia and organ damage involving brain, kidney, heart and GIT. Increased capillary permeability, secondary vasoconstriction and rupture of schizont cause toxin liberation, leading to further organ damage.

Infected RBC also adheres to uninfected RBC to form rosette, causing further blockage. Blood film shows heavy parasites (both schizont and ring form).

Clinical types of pernicious malaria:

- Cerebral type: characterized by high fever, coma without focal neurological signs, convulsion, extensor plantar response. CSF study is normal.
- Algid type: may be gastric, choleric and dysenteric.
- Septicaemic type: characterized by high fever, pneumonia, cardiac failure, renal failure and jaundice.

Treatment: Similar to complicated falciparum (see above).

Q: What is blackwater fever? What is the mechanism, clinical features and treatment of blackwater fever?

A: It is a severe manifestation of falciparum malaria, occurs in previously infected person, characterized by sudden intravascular haemolysis, fever and haemoglobinuria. It is invariably associated with falciparum malaria, in those who had taken antimalarial drugs irregularly or in non-immune person, who had taken irregular antimalarial prophylaxis. It is common in G6PD deficiency.

Mechanism: Actual mechanism is unknown. Autoimmune mechanism may be responsible. Antibodies develop against parasitized and quinized RBCs. With subsequent infection and quinine treatment, there is immunocomplex formation followed by complement mediated massive destruction of both parasitized and nonparasitized RBCs.

Clinical features: High fever with chill and rigor, vomiting, diarrhoea, dark to black urine (haemoglobinuria), collapse and renal failure.

Diagnosis: Mostly clinical and by history. Malarial parasite is not found in blood during attack.

Treatment:

- Similar to complicated malaria.
- Blood transfusion.
- Prednisolone may be helpful.
- Treatment of renal failure.

HEPATOSPLENOMEGALY (DISCUSSION ABOUT KALA-AZAR)

Instruction by the examiner:

- Examine or palpate the abdomen and see the relevants.

Presentation of a Case:

Present as described in hepatosplenomegaly.

Organism: *Leishmania donovani* complex:

- *L. donovani* (India and South East Asia).
- *Leishmania infantum* (Middle East, Mediterranean area).
- *Leishmania chagasi* (South, Central America).

Source/reservoir: Human (Indian kala-azar).

Mode of transmission:

- Bite by infected female sandfly (common).
- Congenital: Transplacental.
- Blood transfusion.

Q: What are the presentations of kala-azar?

A: Incubation period is 1 to 2 months (may be months to years, even 10 years).

- Fever: Usually intermittent, either double or triple rise daily. Sometimes, fever may be irregular, low grade continuous, occasionally undulant fever (pyrexia followed by apyrexial period). There may be chill and rigor.
- Usually no anorexia, no malaise, no coated tongue.
- Bleeding.

Physical findings are:

- Emaciation.
- Anaemia (always present, may be severe).
- Splenomegaly, usually develops early which may be huge (firm to hard in consistency).
- Hepatomegaly, usually develops later.
- Lymphadenopathy: Common in African and Chinese kala-azar, rare in Indian kala-azar.
- Skin: Pigmented, dry thin, scaly. There may be diffuse, warty, non-ulcerative skin lesion containing parasites.

N.B. Remember the following points:

- Human is the only reservoir in Indian subcontinent.
- Other reservoirs include dog, jackal, fox and wild rodents in other country.
- *Leishmania* has two forms: Amastigote and promastigote.
- Amastigote form (oval) is found in human, LD body is found in monocyte-macrophage system.
- Promastigote form (flagellate) is found in sandfly, also in culture media.

Q: What are the mechanisms of anaemia in kala-azar?**A:** Anaemia may be due to:

- Hypersplenism (sequestration and splenic pooling, destruction of RBC in spleen).
- Short lifespan of RBCs.
- Haemolysis.
- Ineffective erythropoiesis, infiltration of marrow by parasite.
- Bleeding, haemodilution.

Q: What are the complications of kala-azar?**A:** As follows:

- Secondary infection (pneumonia, tuberculosis).
- Anaemia.
- Bleeding.
- Gastroenteritis.
- Bacillary dysentery.
- Liver disease (cirrhosis of liver).
- PKDL.
- Rarely, cancrum oris.

Causes of death in Kala-azar: If no treatment is given, patient may die within 1 to 2 year due to:

- Secondary infection.
- Bleeding.

Q: What investigations are done to diagnose kala-azar?**A:** As follows:

1. CBC: It shows anaemia, leucopenia with high lymphocyte and monocyte, thrombocytopenia and high ESR (there is absence of eosinophil). If CBC is repeated after some days, there is **progressive leucopenia** (which is typical in kala-azar).
2. Immunological tests based on antibody:
 - Direct agglutination test (DAT): It is called DAT, because promastigote is used as an antigen. It may be positive after 2 weeks (usually within month). It remains positive years after cure (so it does not indicate active infection).
Disadvantage of DAT: Cannot differentiate the past, subclinical and active infection. False positive DAT may occur in leprosy, African trypanosomiasis, TB and hepatitis B.
 - Immunochromatographical test (ICT): Also called rK39 dipstick rapid test. This test is highly sensitive and also specific.
 - Indirect haemagglutination assay (IHA).
 - Indirect fluorescent antibody test (IFAT).
 - ELISA.
 - Complement fixation test (CFT): It is non-specific, usually positive after 3 weeks. False positive CFT may occur in TB, leprosy, cirrhosis of liver and multiple myeloma. This test is performed by using Kedrowski bacillus.
 - Aldehyde test: Still helpful where there is no facility. This test is positive in 2 to 3 months (negative after 6 months). It is non-specific. False positive may be found in TB, leprosy, cirrhosis of liver, multiple myeloma, SLE, leukaemia and thalassaemia.

3. Detection of antigen: Done by latex agglutination test (Katex) for detecting leishmanial antigen in urine. This test is very simple, more specific than antibody-based test, highly sensitive (96%) and also specific (100%). This test indicates active disease. Antigen is detected in urine within a week and disappears from urine within 3 weeks after successful treatment. So, this test is helpful for early diagnosis and also to see the response to therapy.
4. Definitive diagnosis by isolation of amastigote form Leishman–Donovan (LD) body from bone marrow and spleen puncture. Also done from liver, lymph node and skin lesion. Smears are stained by Leishman, Giemsa or Wright stain. Culture is done in NNN media (Novy–McNeal–Nicolle). LD body is positive as follows:
 - Spleen: 90 to 95% (splenic puncture is avoided in soft spleen, prolonged prothrombin time and platelet $<40,000/\text{mm}^3$).
 - Bone marrow and liver: 85%.
 - Lymph node: 65%.
5. LD body is rarely found in peripheral blood in buffy coat preparation.
6. PCR (from lymph node or bone marrow aspiration), positive up to 100% case.
7. Blood for total protein and A:G ratio (high total protein, low albumin and high globulin).
8. Polyclonal hypergammaglobulinemia, chiefly IgG followed by IgM.

N.B. Culture is done for identification of species and if the number of organisms is less, it may grow in culture media. Organism may grow after 1 week, may take 4 weeks.

Q: Why bleeding occurs in kala-azar?

A: As follows:

- Bleeding may occur before treatment due to thrombocytopenia.
- Bleeding may occur during treatment with sodium stibogluconate.

Q: Why bleeding occurs during treatment with sodium stibogluconate?

A: Actual mechanism is unknown. It may be due to:

- Abnormality in preparation of drug.
- Decomposed or expired date of drug.
- Functional abnormality of platelet by the drug (pentavalent antimony is transformed to trivalent, which may cause thrombasthenia).
- Bleeding due to other causes (CLD or blood dyscrasias).

Q: How to treat if there is bleeding?

A: As follows:

- Drug should be stopped.
- Platelet count, PT, APTT and liver function tests should be done.
- Other causes of bleeding should be looked for.
- Symptomatic treatment should be given, may require blood transfusion.
- After improvement, drug should be started with low dose and then increase the dose (batch of the drug may be changed). If again bleeding, alternative drug may be given.

Q: How to treat kala-azar?**A:** As follows:

1st line therapy: Liposomal Amphotericin B, Miltefosine, Paromomycin or combination therapy.

- Liposomal Amphotericin B: single IV infusion 10 mg/kg.
- Oral drug Miltefosine for 28 days. Age >12 years (50 mg daily if <25 kg body weight and 50 mg twice daily, if >25 kg body weight). Age 2 to 12 years: 2.5 mg/kg body weight in two divided doses, not exceeding 50 mg/day. In a missed dose, the scheduled 28 doses may be taken within 35 days. Avoided in pregnancy due to foetal toxicity. Also avoid in women of child bearing age not using contraceptives regularly, breast feeding women, children less than 2 yrs of age. Helpful in treating resistant kala-azar. Side effects are less, may cause vomiting, diarrhoea, transient rise of SGPT, blood urea nitrogen and creatinine. Not suitable in severe anaemia, undernutrition, known liver and kidney disease.
- Paromomycin: 15 mg/kg/day intramuscularly in the gluteal muscles for 21 days.
- **Combination therapy** (to shorten treatment courses, dose and limit resistance):
 - **1st choice:** Cap. Miltefosine as above mentioned dose for 10 days + Inj. Paromomycin as above mentioned dose for 10 days.
 - **Alternate choice:** Inj. Liposomal Amphotericin B 5 mg/ kg body weight IV single dose on day 1 + Cap. Miltefosine as above mention dose from day 2 up to day 8.
 - Or, Inj. Liposomal Amphotericin B 5 mg/ kg body weight IV single dose on day 1 + Inj. Paromomycin as above mention dose from day 2 up to day 11.

N.B.: Remember the following points:

- *In countries other than Indian subcontinent, Liposomal amphotericin B may be given at 3 mg/kg daily on days 1 to 5, 14 and 21. Dose for immune-incompetent is 4 mg/kg on day 1 to 5, 10, 17, 24, 31 and 38.*
- *Liposomal amphotericin B is expensive and not widely available. Preferable to conventional amphotericin B, as it is more effective, less toxic, less protein bound, concentrated and retained in macrophage-rich organs (RE system) other than kidney (not nephrotoxic). It is safe in pregnancy.*

2nd line therapy: Amphotericin B deoxycholate (conventional) or sodium stibogluconate.

- Conventional amphotericin B: 1 mg/kg for 15 doses, given in slow infusion in 5% dextrose solution 500 cc for 4 to 6 hours daily or on alternate days. It is more protein bound and nephrotoxic. Given after a test dose.
- Sodium stibogluconate: 20 mg/kg for 30 days IV or IM. Can be given in infusion with normal saline. IM injection is very painful, given if there is ECG abnormality (arrhythmia or long QT interval).
- Meglumine antimoniate: 50 mg/kg is an alternative.

General treatment:

- Maintenance of nutrition.
- Correction of anaemia.
- Control of secondary infection, if any.

N.B. Remember the following points while treating with sodium stibogluconate:

- Before starting the therapy, perform renal and hepatic function tests, ECG (to see dysrhythmia, prolonged QT and ischaemia) and chest X-ray (latent TB, pneumonia).
- During IV injection, if the patient complains of chest pain or cough, stop the drug immediately.
- Monitor ECG, CBC including platelet, hepatic and renal functions.
- The drug should be stopped, if there is bleeding, ECG change (arrhythmia, prolonged corrected QT interval).
- No limitation of dose (previously it was thought that dose should not exceed 1 g/day).

Q: What are the **side-effects** of Sodium stibogluconate?

A: Arthralgias, myalgias, raised hepatic transaminases (SGPT), pancreatitis (especially in patients co-infected with HIV). ECG changes (T wave inversion and reduced amplitude), severe cardiotoxicity (concave ST segment elevation, prolongation of QT interval, ventricular dysrhythmias).

Q: How to see the **response** of therapy?

A: As follows:

- Clinical: Improvement of fever, feeling of wellbeing.
- Reduction in the size of spleen (may take months).
- Weight gain.
- Laboratory findings: increased Hb%, total count of WBC and increased albumin.

Q: What do you mean by **relapse kala-azar (RKA)** and **kala-azar treatment failure (KATF)**?

A: As follows:

- The patient who had and treated for KA anytime in the past before one year and diagnosed again as kala-azar is called relapse kala-azar (RKA).
- The patient who had and treated for KA anytime in the past within last one year, but not responded to therapy is called KATF. It is usually due to inappropriate or suboptimal dose or irregular therapy.

Q: How to **treat relapse kala-azar (RKA)** or **kala-azar treatment failure (KATF)**?

A: As follows:

- KATF and RKA cases should be treated with alternative 1st line agent (e.g., Patient who received Liposomal Amphotericin B, then should be treated with Miltefosine or Paromomycin or combination).
- If alternative 1st line agents are not available, then a 2nd line agent should be used.

Q: How to **treat kala-azar in pregnancy**?

A: Risk of treatment should be weighed against benefit. Treatment should be given according to the severity. Drug of choice is Liposomal Amphotericin B (5 mg/kg body weight on alternate days for 3 doses).

Treatment should be given as follows:

- If diagnosed at 1st trimester, then it should be treated at 2nd trimester.
- If diagnosed at 3rd trimester, then it should be treated after delivery.
- Miltefosine and Sodium stibogluconate is contraindicated in pregnancy.

POST-KALA-AZAR DERMAL LEISHMANIASIS (PKDL)

Instruction by the examiner:

- Perform the general examination or look at the face. What are your findings?

Presentation of a Case:

- There are multiple, pale, pink, reddish, wart like nodules of variable size and shape involving nose, cheek and ear lobule.
- Skin is thick.

My differential diagnoses are:

- PKDL.
- Lepromatous leprosy.
- SLE.
- Dermatomyositis.
- Sarcoidosis.
- MCTD.
- Neurofibromatosis.
- Others: Lipomatosis, acne rosacea, leukaemia cutis, secondary syphilis and rhinophyma (in which there is irregular thickening of skin of nose with enlarged follicular orifice).

Q: Ask **one question** to the patient.

A: Previous history of kala-azar.

Q: What is the more likely **diagnosis** in this case?

A: More likely diagnosis is PKDL.

Q: What is **PKDL**?

A: It is non-ulcerative, cutaneous lesion that occurs after successful treatment of visceral leishmaniasis. Initially starts as macules, then erythematous patches, followed by wart-like nodular lesions on the face, ear lobules and limbs. Amastigotes are scanty in the lesion.

Following treatment, visceral infection disappears, but organisms may remain in skin. After a variable period, skin resistance is lost with resurgence of old infection, causing PKDL.

In India, it occurs in a small minority of patients, 6 months to 3 years or more after the initial infection, creating a persistent human reservoir. The patient usually presents with macules, papules, nodules (most common) and plaques on the face, mainly around the chin. The face is often erythematous. Hypopigmented macules can occur over all parts of the body and are highly variable in extent and location. Usually, no systemic symptoms and no spontaneous healing.

In Sudan, about 50% develop skin manifestations of PKDL concurrently with visceral leishmaniasis or within 6 months afterwards. The skin features are as above. In addition, there may be measles like micro-papular rash all over the body. Children are more frequently affected than in India. Spontaneous healing occurs in about three-fourth cases within 1 year.

Q: What are the **presentations** of PKDL?

A: In early case, depigmented macules, erythematous, well-circumscribed lesions may be seen. Later, wart like nodules, or only multiple nodules of variable sizes and shapes are seen involving nose, cheek and ear lobule.



Early PKDL (depigmented macules)



Early PKDL (few nodules)



PKDL (nodules)



PKDL (multiple nodules)

Q: What investigation is done to diagnose PKDL?

A: As follows:

- Demonstration of amastigote form of LD body in lesions by slit-skin smear and culture. Smear is prepared from nodular lesions (LD bodies are not found in depigmented lesion).
- Immunofluorescence and immunohistochemistry may demonstrate the parasite in skin tissue.
- In the majority of patients, serological tests (DAT or rk39 strip tests) are positive. It is not helpful for diagnosis.

Q: How to treat PKDL?

A: As follows:

First line treatment: Usually miltefosine should be given:

- **Adult:** 50 mg twice daily for 12 weeks.
- **Children:** 2.5 mg/kg daily in two divided doses for 12 weeks (not exceeding 50 mg/day).

Second line treatment:

- Amphotericin B deoxycholate: 1 mg/kg IV daily or alternative days for 15 doses in 1 cycle. 6 cycles are given with 10 days gap after each cycle.
- Or, Sodium Stibogluconate: 20 mg/kg daily IM for 20 days in 1 cycle. 6 cycles are given with 10 days gap after each cycle.
- In Sudan, sodium Stibogluconate for 2 months is considered adequate.

HEPATOMEGALY (ISOLATED)

Instruction by the examiner:

- Examine or palpate the abdomen.

Presentation of a Case:

- The liver is enlarged, . . . cm from costal margin in the right midclavicular line.
- Margin is sharp (or rounded).
- Surface is smooth (or irregular).
- Tender (or non-tender).
- Firm (or hard or soft in consistency).
- Upper border of liver dullness is in right . . . intercostal space (mention the site) in right mid-clavicular line.
- There is (no or yes) hepatic bruit (or rub).

My diagnosis is **Hepatomegaly**.

Q: What are the **causes** of hepatomegaly in this case?

A: Mention according to your findings.

1. If huge hepatomegaly (firm or hard), the causes are:

- Hepatoma.
- Secondaries in the liver.
- Cirrhosis of liver (primary biliary cirrhosis, haemochromatosis and alcoholic cirrhosis in early stage).
- CCF.
- Polycystic liver.
- Hydatid cyst.
- Amyloidosis.

2. If hard and nodular, the causes are:

- Hepatoma.
- Secondaries in the liver.
- Hydatid cyst.
- Polycystic liver.
- Others (amyloidosis, occasionally, macronodular cirrhosis of liver).

3. If firm hepatomegaly with irregular surface, causes are:

- Multiple secondaries.
- Hydatid cyst.
- Macronodular cirrhosis.
- Sarcoidosis.
- Amyloidosis.

4. If enlarged, tender liver, the causes are:

- Viral hepatitis.
- Liver abscess (pyogenic or amoebic).
- Congestive cardiac failure (CCF).
- Chronic constrictive pericarditis.
- Budd–Chiari syndrome.
- Cholangiohepatitis.

5. If soft or slightly firm with smooth surface, non-tender liver:

- Malaria.
- Kala-azar.
- Enteric fever.
- Myeloproliferative disease.
- Lymphoproliferative disease (lymphoma, CLL and multiple myeloma).
- Sarcoidosis.

6. Cause of enlargement of the left lobe:

- Hepatoma.
- Secondary in the liver.
- Hydatid cyst.
- Liver abscess (if tender).

Q: Mention **one** investigation that is helpful for the diagnosis.

A: Ultrasonography of hepatobiliary system.

Q: Why it is liver?

A: Because:

- The mass is in the right hypochondrium and in the epigastrium (left lobe).
- Moves with respiration.
- Get above the swelling is not possible.
- Well defined lower margin, which is parallel with the costal margin.
- Percussion is dull over it, which is continuous in lower part of chest.

Q: Can liver be palpable without hepatomegaly?

A: Yes, if it is pushed downward by any pathology in the right side of chest, such as emphysema, pleural effusion or pneumothorax. It is normally palpable in neonate.

Q: Why is it tender?

A: Due to stretching of Glisson's capsule.

Q: What are the causes of hepatic bruit?

A: As follows:

- Hepatoma (commonest cause, due to increased vascularity).
- Acute alcoholic hepatitis.
- AV fistula in liver (due to trauma or iatrogenic in liver biopsy).
- Haemangioma of the liver.

Q: What are the causes of hepatic rub?

A: As follows:

- Secondary deposit in the liver.
- Trauma.
- Infarction.
- Perihepatitis in pelvic inflammatory disease (gonococcal or chlamydial in females, called Fitz–Hugh–Curtis syndrome).

Q: What **else** do you want to see, if liver is enlarged and tender?

A: As follows:

- Jaundice (in viral hepatitis).
- Engorged and pulsatile neck veins, dependent pitting oedema (in CCF). Also to see heart (in CCF, chronic constrictive pericarditis).
- Tenderness and oedema in right lower chest (in liver abscess).
- History of fever (Liver abscess).
- History of drug (hepatitis).

Q: What are the causes of **pulsatile liver**?

A: As follows:

- Tricuspid regurgitation (commonest).
- Vascular anomaly (haemangioma).
- AV fistula (during biopsy or traumatic).

Q: What are the causes of **hepatomegaly in cardiac diseases**?

A: As follows:

- CCF.
- Pericardial effusion.
- Chronic constrictive pericarditis.
- Cardiomyopathy secondary to alcoholism, haemochromatosis, amyloidosis.

Q: What are the causes of **hepatomegaly associated with jaundice**?

A: As follows:

- Acute viral hepatitis.
- Weil's disease.
- Haemolytic anaemia.
- Obstructive jaundice.

Q: What **investigations** do you suggest?

A: Investigations should be done according to the history and suspicion of cause:

1. USG of whole abdomen (first preferred test).
2. CBC (leucocytosis in pyogenic liver abscess).
3. If viral hepatitis is suspected:
 - Serum bilirubin, SGPT, alkaline phosphatase, prothrombin time.
 - Viral markers for Hepatitis B (HBsAg, HBeAg and anti-HBc), anti-HEV for Hepatitis E, anti-HAV for Hepatitis A and anti-HCV for Hepatitis C.
4. If CLD is suspected:
 - Total protein, A:G ratio and prothrombin time, also viral markers (for HBV and HCV).
 - Endoscopy (to see oesophageal varices).
 - Proctoscopy (to see haemorrhoid in CLD).
 - CT or MRI.
 - Liver biopsy.
5. If hepatoma—check for α -foetoprotein. If secondary, other tests to see the primary source.
6. If hydatid cyst or cardiac cause, investigate accordingly.

Q: How liver biopsy is done?

A: 4 methods:

- Percutaneous (by Vim–Silverman needle, Menghini needle or Tru-cut needle).
- Transjugular (if PT is prolonged and platelet count is low).
- Laparoscopy (if there is bleeding, it can be stopped easily through laparoscope).
- During laparotomy (if done for other reason).

Q: What measures should be taken before doing liver biopsy?

A: As follows:

- Consent and co-operation of the patient.
- Exclude biliary obstruction, marked ascites, severe anaemia and high bilirubin.
- Prothrombin time should be normal (not more than 4 seconds that of control).
- Activated partial thromboplastin time should be normal.
- Platelet count should not be $<100,000/\text{mm}^3$.

Follow-up after biopsy:

- Complete bed rest for 24 hours.
- Regular monitoring of pulse and BP.
- Blood should be kept ready for transfusion, if necessary.

N.B. If bilirubin is high, liver biopsy should not be done, as liver tissue does not take the stain.

Q: What are the complications of liver biopsy?

A: As follows:

- Bleeding.
- Pain (may radiate to shoulder).
- Rarely, biliary peritonitis and pneumothorax.

Q: What is liver span?

A: By percussion, upper border of liver dullness is in the sixth intercostal space or rib in right midclavicular line and the distance between this upper border and lower border is called liver span. Normally, it is less than 13 cm.

FITZ–HUGH–CURTIS SYNDROME

Fitz–Hugh–Curtis syndrome is caused by *Chlamydia* or *Gonococcus* infection, which tracks up the right paracolic gutter to cause perihepatitis, secondarily from endocervical or urethral infection. It is characterized by fever, pain in the right hypochondrium with radiation to right shoulder, tender hepatomegaly, hepatic rub and small right pleural effusion. (*Chlamydia* infection is asymptomatic in 80% cases).

Investigations: endocervical swab for microscopy and special culture, direct fluorescent antibody for *Chlamydia*, ELISA and PCR may be performed.

Treatment: Tetracycline or doxycycline or erythromycin or azithromycin are used for *Chlamydia* infection.

HEPATOMEGALY (DISCUSSION ABOUT HEPATOMA)

Instruction by the examiner:

- Examine or palpate the abdomen.

Presentation of a Case:

- The liver is enlarged, . . . cm from the costal margin in right mid-clavicular line.
- Margin is irregular.
- Surface is irregular and nodular.
- Non-tender, hard in consistency.
- Upper border of liver dullness in . . . intercostal space in right midclavicular line.
- There is hepatic bruit.

My differential diagnoses are:

- Hepatoma.
- Secondary deposit in liver.
- Others: Hydatid cyst, polycystic liver.

Q: Why is this hepatoma?

A: Because, the liver is hard, irregular, nodular, non-tender and there is hepatic bruit.

Q: Why not secondary deposit?

A: In secondary deposit, the nodules are usually multiple and small. There may be umbilication but no hepatic bruit. (There may be history of primary carcinoma elsewhere in the body).

Q: How to suspect that hepatoma has developed in CLD or cirrhosis of liver?

A: In the following way:

- Rapid deterioration of general condition.
- Pain in right hypochondrium.
- Increasing ascites, not responding to usual therapy.
- Enlarging liver with appearance of nodule (hard and irregular).
- Presence of bruit.
- Biochemically increase α -foetoprotein.

Q: What are the clinical features of HCC?

A: As follows:

- May be asymptomatic.
- History of CLD or hepatitis B or C infection.
- Weight loss, anorexia and pain in right hypochondrium. Rapid development of these features in a cirrhotic patient is suggestive of HCC.
- On examination, an enlarged, irregular, tender liver may be felt with hepatic bruit.

Q: What are the screening tests to detect hepatoma in cirrhosis of liver?

A: USG and α -foetoprotein. USG every 3 to 6 months in high risk group (B and C infection, alcoholic cirrhosis and haemochromatosis).

Q: What are the causes of hepatoma?

A: As follows:

- Chronic hepatitis B infection. HCC is four times common in those with HBeAg positive than those with HBsAg alone. 75 to 90% are associated with cirrhosis of liver.
- Chronic hepatitis C infection. Risk of HCC is higher in HCV than HBV. Usually associated with cirrhosis.
- Cirrhosis of liver due to any cause such as alcoholic cirrhosis, non-alcoholic steatohepatitis (NASH), haemochromatosis, Wilson's disease, α_1 -antitrypsin deficiency and primary biliary cirrhosis. Macronodular cirrhosis is more prone to develop hepatoma.
- Aflatoxin by fungus *Aspergillus flavus* (from contaminated ground nut grain stored in tropical condition).
- Chronic arsenicosis.
- Clonorchis sinensis (a parasitic infection).
- Prolonged androgen therapy, anabolic steroid and oral contraceptive pill (oestrogen) may cause hepatoma (usually adenoma, rarely hepatoma).
- Smoking (rare).

Q: How to differentiate between primary carcinoma (hepatoma) and secondary carcinoma?

A: As follows:

Primary	Secondary
1. History of hepatitis B or C infection or cirrhosis of liver or any CLD	1. History of primary carcinoma (in GIT, bronchus, breast, thyroid and kidney). No primary source in 50% cases
2. Nodule usually single	2. Usually multiple nodules
3. No umbilication over the nodule	3. Umbilication over the nodule (due to necrosis)
4. Bruit present (due to increased vascularity)	4. No bruit (because of necrotic lesion)
5. Rub may be present	5. Rub is more common
6. Investigations • α-foetoprotein is increased • Alkaline phosphatase is slightly increased • CEA is normal	6. Investigations • α-foetoprotein usually not increased • Alkaline phosphatase is high • CEA is increased

Q: What investigations are done to diagnose hepatoma?

A: As follows:

1. USG (shows mass in 90% of cases).
2. α -fetoprotein: High (60%), normal (one-third). Levels increase with the size of tumour.
3. Others:
 - CT or MRI.
 - Serum CEA (high in secondaries).
 - Plain X-ray of abdomen to see calcification in liver (sunburst calcification).
4. Liver biopsy under USG control (This is confirmatory but avoided in patient eligible for transplantation or surgical resection because of small risk of tumour seeding along the needle tract).
5. Viral markers (HBV and HCV).

N.B. Metabolic abnormalities are polycythaemia, hypercalcaemia, hypoglycaemia and porphyria cutanea tarda.

Q: What are the other **primary** tumours of liver?

A: Rarely, fibrolamellar hepatocellular carcinoma, common in young adults, affecting equally in male and female, in the absence of hepatitis B and cirrhosis. The tumour is large at presentation, α -foetoprotein is normal. It is treated by surgical resection. Other (rare) primary tumours are haemangioendothelial sarcoma, cholangiocarcinoma, hepatoblastoma, leiomyosarcoma, fibrosarcoma.

Q: What are the **benign** tumours of liver?

A: As follows:

- Haemangioma is the commonest. Rarely causes symptom. No treatment is required.
- Adenoma, more in females, caused by oestrogen containing oral contraceptives, androgen and anabolic steroid. Surgical resection, if pressure symptoms, also if pregnancy is desired (as size is increased in pregnancy).
- Focal nodular hyperplasia.
- Fibroma.
- Leiomyoma.

Q: Why **secondary carcinoma** is more common in the liver?

A: Because liver has dual blood supply causing relatively more blood flow (by portal vein and hepatic artery).

Q: How to **treat** hepatoma?

A: As follows:

- Surgical resection in non-cirrhotic patient. Recurrence is 50% at 5 years.
- In cirrhotic patient, resection may be done with small tumour and good liver function.
- Liver transplantation (5 year survival is 70% with single tumour <5 cm, or 3 tumours <3 cm). Hepatitis B and C may recur in transplanted liver.
- Percutaneous injection of ethanol, if tumour size is 3 cm or less, 80% cure rate. Recurrence is 50% at 3 years. Repeated injection may be given. It causes tumour necrosis.
- Transcatheter radiofrequency ablation (RFA) using a single electrode inserted into the tumour under radiological guidance.
- Transcatheter hepatic arterial embolization (transarterial chemoembolization—TACE) by Gelfoam and doxorubicin. TACE is contraindicated in decompensated cirrhosis and multifocal HCC.
- Chemotherapy: Doxorubicin is effective in 30% cases. Sorafenib, a multikinase inhibitor. Prolongs survival to 10 months in patient with non-resectable tumours.

Q: What is **α -foetoprotein**?

A: It is a normal component of plasma protein, produced by the foetal liver older than 6 weeks and reaches maximum concentration at 12 to 16 weeks of foetal life. It falls few weeks after birth. Reappearance in blood in adult is pathognomonic.

Q: What are the **causes** of high α -foetoprotein?

A: As follows:

1. Hepatoma (commonest), may be very high >500 ng/mL. Level increases with size. It may be normal in small sized tumour.
2. Other causes:
 - Chronic active hepatitis (indicates hepatocellular regeneration).
 - Acute viral hepatitis (indicates hepatocellular regeneration).
 - Acute hepatic necrosis due to paracetamol toxicity.
 - Embryonic tumours of the ovary and testis.
 - Embryonic hepatoblastoma.
 - Rarely, in other malignancy—carcinoma of stomach, pancreas, bile duct and gall bladder (usually with large metastasis in liver).
 - During pregnancy (in serum and amniotic fluid). High level indicates neural tube defect (meningomyelocele or anencephaly). It is an indication for termination of pregnancy.

HEPATOMEGALY (ENLARGED TENDER LIVER, VIRAL HEPATITIS)

Instruction by the examiner:

- Examine or palpate the abdomen.

Presentation of a Case:

- Liver is enlarged, . . . cm from the costal margin in right midclavicular line.
- Margin is sharp, surface is smooth, tender, soft in consistency, upper border of liver dullness is in right, . . . intercostal space (mention location) and no hepatic bruit or rub.

My diagnosis is **tender hepatomegaly**, which may be due to:

- Acute viral hepatitis.
- Liver abscess.
- CCF.
- Chronic constrictive pericarditis.
- Weil's disease.

Q: If it is viral hepatitis, what **else** do you want to see?

A: Jaundice.

Q: What are the causes of **acute hepatitis**?

A: As follows:

- Acute viral hepatitis.
- Drugs: Paracetamol, alcohol.
- Non-viral infection: *Toxoplasma gondii*, *Leptospira icterohaemorrhagiae*, *Coxiella burnetii* (Q fever).
- Others: Pregnancy, Wilson's disease, poisons (amanita phalloides mushroom, aflatoxin, carbon tetrachloride).

Q: What are the **viruses** causing hepatitis?

A: As follows:

1. Hepatitis A, B, C, D and E virus.
2. Other viruses:
 - Epstein–Barr virus.
 - CMV.
 - Herpes simplex virus.
 - Yellow fever virus.
 - Dengue virus.

N.B.: Remember the following points:

- *Hepatitis D is a RNA-defective virus, can infect only with HBV or can superinfect in HBV carriers.*
- *Only B virus is DNA type, all others are RNA type.*

Q: What **history** do you like to take in viral hepatitis?

A: As follows:

1. Anorexia, nausea and vomiting.
2. Pain (usually in right hypochondrium).
3. Yellow or high coloured urine, yellow eye and body.
4. Itching, pale stool (due to intrahepatic cholestasis).
5. History of (for HBV and HCV):
 - Injection or infusion of blood and blood products, any fluid.
 - Sharing of injection syringe by others or parenteral drug abusers.
 - Close contact with infected person.
 - Acupuncture or tattooing.
 - Homosexuality.
 - Organ transplantation.
 - Newborn of infected mother with HBV or HCV.
 - Chronic haemodialysis.
 - Travel to other parts.

N.B. Remember the following points:

- *Clinical features and pathological features are same by all viruses. They differ in their tendency to cause acute and chronic infections.*
- *HBV and HCV may cause chronic hepatitis,*
- *Hepatitis D virus (HDV) can cause chronic infection with HBV.*
- *HAV and hepatitis E virus (HEV) are not associated with chronic infection.*

Q: What are the **clinical features or presentations** of acute viral hepatitis?

A: As follows:

- Anorexia, nausea, vomiting.
- Yellow colouration of skin and sclera, high-coloured urine.
- Fever, malaise, weakness.
- Pain in the right upper abdomen,
- Pale stools may develop later (due to intrahepatic cholestasis).

N.B.: Other features:

- *In hepatitis due to B virus: some extra features may be present, such as serum sickness like illness—skin rash (urticaria, maculo-papular rash), polyarthritis affecting small joints, fever, extrahepatic immune complex mediated arteritis or glomerulonephritis.*

Q: What are the **markers** of HBV infection?

A: As follows:

- HBsAg.
- HBeAg (indicates active replication. If persists for >6 months, it indicates chronic infection).
- Anti-HBc (IgM type indicates acute infection).
- HBV DNA.

Q: What are the **markers** of B virus replication?

A: HBeAg, HBV DNA.

Q: What **investigations** do you suggest in acute viral hepatitis?

A: As follows:

1. LFTs:
 - Serum bilirubin: High.
 - SGPT: High.
 - SGOT: High (also SGOT is high in drug-induced hepatitis).
 - Alkaline phosphatase: may be high (slightly high due to intrahepatic cholestasis, rarely more than twice the upper limit. But in cholestatic hepatitis or obstructive jaundice, alkaline phosphatase may be very high).
 - Prothrombin time: Prolonged in severe hepatitis.
2. Viral markers:
 - Virus A (anti-HAV, IgM indicates acute infection).
 - Virus B (HBsAg, HBeAg, anti-HBc). In acute infection, HBsAg may be cleared rapidly, anti-HBc IgM is diagnostic.
 - Virus E (anti-HEV, IgM indicates acute infection).
 - Virus C (anti-HCV).
3. USG of hepatobiliary system.
4. Others: CBC (may be leucopenia, with lymphocytosis), blood sugar, urine routine examination (in Weil's disease, there may be proteinuria, cast, RBC etc.).

N.B. Remember the following points:

- HBsAg appears in the blood 6 weeks to 3 months after acute infection, then disappears.
- HBeAg rises early and declines rapidly.
- Anti-HBc—high titres of IgM suggest acute infection and viral replication. It persists for many months.
- Anti-HBsAg appears late and indicates immunity.
- Anti-HBe appears after anti-HBc, indicates decreased infectivity.

Q: How would you **treat** acute viral hepatitis?

A: No role of anti-viral therapy, even for hepatitis B. Treatment is symptomatic and supportive.

- Bed rest.
- Normal diet.
- Supportive and symptomatic.
- Avoid sedative, opium and alcohol, other hepatotoxic drugs.

Q: What is the **prognosis** of acute viral hepatitis?

A: It depends on the type of the virus:

1. HAV:
 - Good, recovery in 3 to 6 weeks.
 - Rarely (0.1%) develop acute liver failure.
 - Mortality in young adult is 0.1% from acute fulminating hepatic failure. Mortality increases with age.

2. HBV:

- In 90 to 95% cases, full recovery occurs within 6 months.
- 5 to 10% develop chronic infection. Most remain as inactive HBV infection. In some, cirrhosis of liver and hepatoma may develop after many years. Cirrhosis usually develops in 15 to 20% cases in 5 to 20 years. This proportion is higher in those with HBeAg positive.
- Fulminating hepatic failure may develop in <1%.
- Infection from mother to child during pregnancy causes chronic infection in child (90%), recovery is rare.
- Chronic infection is also common in Down's syndrome and HIV infection.

3. HCV:

- Rarely causes acute infection.
- Commonly causes chronic hepatitis.

4. Combined HBV and HDV infection can cause more aggressive disease.

5. HEV:

- Similar to HAV.
- Hepatitis E infection is serious during pregnancy, can cause acute liver failure with high mortality.

Q: What are the complications of acute viral hepatitis?

A: As follows:

- Acute fulminating hepatic failure (by B and sometimes E in pregnancy. It is rare by HAV).
- Relapsing hepatitis. May be clinically evident (5 to 15%) or, more commonly biochemically detectable. It settles spontaneously.
- Cholestatic hepatitis mostly by HAV, may persist for 7 to 20 weeks.
- Post-hepatitis syndrome. It is seen in anxious patient who complains of malaise, anorexia, nausea, vomiting, right hypochondrial pain or discomfort in the absence of clinical or biochemical evidence of liver disease. Reassurance is necessary.
- CLD (due to B and C), which may lead to cirrhosis of liver and hepatoma.
- Others: Aplastic anaemia (usually reversible), rarely Coombs positive haemolytic anaemia, polyarthritis nodosa, Henoch-Schönlein purpura, glomerulonephritis and collagen vascular disease.

Q: What are the causes of chronic hepatitis?

A: As follows:

- Virus: HBV, HCV, combined HBV and HDV.
- Autoimmune.
- Drugs: Methyldopa, isoniazid, ketoconazole, nitrofurantoin.
- Alcohol.
- Hereditary: Wilson's disease, haemochromatosis, α_1 -antitrypsin deficiency.
- Inflammatory bowel disease (commonly ulcerative colitis).

Q: What should be done in a person with incidental HBsAg positive?

A: Incidental HBsAg positive patient should have investigations such as HBeAg, anti-HBe, HBV-DNA and SGPT. Most patients remain asymptomatic as chronic HBV healthy carrier. In many cases, there is no active liver disease, normal or slightly raised transaminase and the patient is not highly infective, do not develop progressive liver disease although some patients develop reactive hepatitis. There is an annual spontaneous clearance rate of HBsAg of 1 to 2%.

No treatment is necessary. Only regular follow up and reassurance is needed.

Q: What are the indications for treatment in chronic HBV infection?

A: Indications for therapy are similar for HBeAg-positive and negative patients with chronic hepatitis. 3 criteria are used: serum HBV DNA levels, serum ALT levels and histological grade and stage.

- Patients with HBV DNA above 2000 IU/mL and/or ALT above the upper limit of normal with moderate to severe active necroinflammation and/or fibrosis in the liver biopsy should be given anti B viral therapy.
- If cirrhosis is present, treatment should be given, independent of ALT or HBV DNA levels. Decompensated cirrhosis can also be treated with oral antiviral agents, but liver transplantation may be required.
- All patients, regardless of disease phase, need long-term follow-up, as transition to an active phase is common. Lifetime risk of malignancy is increased in all patients who are HBsAg-positive.

BRIEF DISCUSSION ABOUT WEIL'S DISEASE (LEPTOSPIROSIS)

Def: It is a leptospiral disease caused by *Leptospira icterohaemorrhagiae* characterized by high fever, jaundice, haemorrhage and renal impairment. Sewerage workers, fisherman, farmers are prone to leptospirosis.

Mode of infection: By contact with infected rat urine.

Incubation period: 7 to 14 days.

Organism and animal hosts of different types of Leptospirosis:

- *Leptospira icterohaemorrhagiae* of rat (rodent).
- *Leptospira pomona* of pigs and cattle.
- *Leptospira canicola* of dogs and pigs.
- *Leptospira hardjo* of cattle.

Leptospirosis is caused by the spirochaete *Leptospira interrogans*. Rodents, particularly rats, are the most important reservoir of infection. The organism is excreted in the urine and may survive in the soil for several weeks. Entry into the human host is through cuts and abrasions on the skin, or through intact mucous membranes or contaminated water.

Pathology: Replication occurs in the blood, tissue and multisystem involvement may occur. Kidney and liver are commonly affected. In kidney, there may be acute interstitial nephritis and tubular necrosis. In liver, centrilobular necrosis in severe case.

Clinical features: 2 phases:

1. **Initial or septicaemic phase**—Persists for 4 to 7 days, characterized by high fever, headache, myalgia, abdominal pain, anorexia, nausea, vomiting, skin rash (macular, maculopapular or haemorrhagic), conjunctival injection (blood-shot eyes). Proteinuria and haematuria may be present.

In severe case, renal impairment (due to impaired renal perfusion and acute tubular necrosis, manifested as oliguria or anuria). 90% cases are anicteric, jaundice and impairment of liver function are present in severe cases. Lung involvement is common, there is dry cough, haemoptysis, bilateral lung consolidation and ARDS with multiorgan dysfunction may occur. Haemorrhage (epistaxis, haematemesis, melaena) may occur. Liver failure, myocarditis, cardiac failure, encephalitis, aseptic meningitis, meningism, may occur. Haemolytic anaemia, thrombocytopenia, uveitis, haemolytic uremic syndrome may occur. Hepatosplenomegaly is present in 20% cases.

2. **Second or immune phase**—There is development of antibody and leptospira disappears from blood. It lasts for 2 to 5 days. Features are usually mild, but meningism or aseptic meningitis and iridocyclitis may occur. Majority recover uneventfully.

N.B. Any case with high fever and combination of hepatitis, renal failure, bleeding manifestations and carditis is highly suggestive of Weil's disease.

Investigations:

- CBC: polymorphonuclear leucocytosis. Thrombocytopenia in severe case.
- Blood culture (Fletcher media): Positive in first week (within 4 days of illness).
- Urine R/E: Proteinuria, haematuria, RBC cast.
- Urine culture for leptospira in second week.
- LFT: High bilirubin, SGPT and prolonged prothrombin time.
- Serum CPK is high.
- Serological test: Microscopic agglutination test (MAT) positive (4 fold rise) at the end of 1st week. IgM ELISA, immunofluorescence technique, rapid immunochromatographic test etc. may be done.
- CSF study: Abnormal in 90% cases.
- PCR: Detection of leptospiral DNA by PCR is possible in blood in early symptomatic disease, in urine from 8th day of illness and for many months thereafter.

Treatment:

1. **Antibiotic should be started as early as possible in suspected case:**
 - Doxycycline (100 mg 12 hourly for 1 week).
 - In severe case—IV benzyl penicillin (1.5 million units 6 hourly for 1 week) or Ceftriaxone (1 g daily for 1 week).
2. In renal failure and jaundice:
 - Fluid and electrolyte balance must be maintained.
 - Dialysis may be needed.
 - Exchange transfusion may be needed in severe hyperbilirubinaemia.
3. If anaemia and thrombocytopenia: Blood transfusion may be needed.

TENDER HEPATOMEGALY (DISCUSSION ABOUT LIVER ABSCESS)

Instruction by the examiner:

- Examine or palpate the abdomen and see the relevants.

Presentation of a Case:

Present as in viral hepatitis.

Add—Local oedema and fullness of intercostal space in right lower chest with local intercostal tenderness in right lower chest called punch tenderness.

My diagnosis is **tender hepatomegaly**, which may be due to:

- Acute viral hepatitis.
- Liver abscess.
- CCF.
- Chronic constrictive pericarditis.
- Weil's disease.

Q: What **else** do you like to see in liver abscess?

A: As follows:

- Local oedema and fullness of intercostal space in right lower chest.
- Local intercostal tenderness in right lower chest called 'punch tenderness'.
- Patient may have high temperature and looks toxic.

Q: What are the **types** of liver abscess?

A: 2 types:

- Pyogenic liver abscess.
- Amoebic liver abscess.

Q: What are the **causes of pyogenic** liver abscess?

A: As follows:

- Ascending cholangitis in biliary obstruction (common bile duct) by stone, stricture and neoplasm or spreads from empyema of gall bladder.
- Haematogenous.
- Portal pyaemia (mesenteric infection) from intra-abdominal sepsis (suppurative appendicitis, perforation).
- Septicaemia or bacteraemia (along the hepatic artery).
- Direct extension from peripheral abscess.
- Trauma.
- Infection of liver tumour or cyst.
- Dental sepsis.

Q: What are the **organisms**?

A: *E. coli*, *Strepto. milleri*, *Strepto. faecalis*, other *Streptococcus* species, *Staph. aureus*, *Proteus vulgaris*, anaerobic organisms or bacteroids (from large bowel). Often the infection is mixed.



Liver abscess (fullness of intercostal space)



Liver abscess (swelling in right lower chest)

Q: What are the features of pyogenic liver abscess?

A: Features of pyogenic liver abscess:

- Pyogenic abscess are usually multiple and small. Single abscess may occur in right lobe, multiple abscesses are due to infection secondary to biliary obstruction. Immunocompromised patients are likely to develop pyogenic liver abscess.
- Fever, may be very high with chill and rigor.
- Malaise, anorexia, nausea and weight loss.
- Abdominal pain, mainly in right upper abdomen, may radiate to right shoulder.
- Pleuritic right lower chest pain (may be small pleural effusion, pleural rub).
- Jaundice is usually mild, may be severe in multiple abscesses causing biliary obstruction.
- Sometimes, only pyrexia of unknown origin (PUO) may be present.
- Complications include rupture, secondary infection and septicaemia.

Q: What are the features of amoebic liver abscess?

A: Features of amoebic liver abscess:

- Amoebic liver abscess is usually large, single and located in right lobe. Multiple abscesses may occur in advanced disease.
- History of diarrhoea or intestinal disease (absent in 50% cases).
- Fever (low grade), PUO may be the only presentation.
- Pain in right hypochondrium.
- Toxicity is absent.

Q: What is the character of pus in amoebic liver abscess?

A: Chocolate or anchovy sauce colour.

Q: What are the **differences** between pyogenic and amoebic liver abscess?

A: As follows:

Points	Pyogenic	Amoebic
1. Organism	<i>E. coli</i> and others	<i>Entamoeba histolytica</i>
2. History	Cholangitis, septicaemia	Amoebiasis
3. Symptoms	High fever with chill and rigor	Fever mild to moderate, no chill and rigor
4. Neutrophil leucocytosis	Common	Less
5. Ultrasonography	Usually multiple	Usually single
6. Aspiration	Frank pus	Chocolate or anchovy sauce
7. Prognosis	More fatal	Less fatal

Q: What **investigations** do you suggest in liver abscess?

A: As follows:

1. CBC (leucocytosis in pyogenic liver abscess).
2. LFT (high alkaline phosphatase, high bilirubin in 25%. SGPT, SGOT are usually normal or slightly high).
3. Serum albumin (low).
4. Chest X-ray (shows raised right dome of diaphragm, small right sided pleural effusion or collapse of right lung).
5. Blood for C/S (in pyogenic, positive in 30% cases. In some study, 50 to 80% cases were positive).
6. USG of whole abdomen.
7. CT scan (shows multiple bull's-eye appearance) or MRI of abdomen may be done.
8. If needed, USG-guided aspiration of pus for C/S (in pyogenic). Amoebae are rarely found in pus.
9. For amoebic liver abscess:
 - Stool for RME (to see trophozoites and cysts), also C/S (positive in 25% cases).
 - Lectin antigen (positive in serum, liver pus or saliva but not in stool).
 - ELISA (to detect antigen).
 - Immunofluorescent antibody test (positive in 95%).
 - Indirect haemagglutination test (positive in 95%).
 - Complement fixation test.
 - PCR from liver pus (100% sensitive).
 - Sigmoidoscopy in some cases (which shows flask shaped ulcer).

Q: How to **treat pyogenic liver abscess**?

A: As follows:

- Antibiotic: amoxicillin plus gentamicin **plus** metronidazole for 2 to 3 weeks, may be up to 6 weeks.
- If large (>5 cm) or not responding to antibiotic therapy—USG-guided aspiration should be done.
- Surgical drainage is rarely needed. Even more rarely hepatic resection may be indicated for chronic persistent abscess or pseudo-tumour.
- Treatment of underlying cause like biliary obstruction.

Q: How to treat amoebic liver abscess?

A: As follows:

- Metronidazole 800 mg 8 hourly for 10 days or secnidazole 2 g daily for 5 days or tinidazole or ornidazole 2 g daily for 3 days.
- Nitazoxanide 500 mg 12 hourly for 3 days.
- Diloxanide furoate 500 mg 8 hourly for 10 days or paromomycin should be given for intestinal infection, given after the treatment of amoebic liver abscess to eradicate luminal cyst.
- USG-guided aspiration should be done if abscess is large (>5 cm) or if there is no response to medical therapy or if there is risk of rupture.

N.B. Remember the following points:

- *Mixed infections may be found in many cases. Hence, antibiotic plus anti-amoebic drugs may be needed.*
- *Abscess may rupture into pleural cavity, pericardial sac or peritoneal cavity. In such cases, immediate aspiration or surgical drainage is needed.*

HEPATOMEGALY (DISCUSSION ABOUT HYDATID CYST)

Instruction by the examiner:

- Examine or palpate the abdomen.

Presentation of a Case:

- The liver is enlarged, . . . cm from the costal margin in right mid-clavicular line.
- Margin is rounded.
- Surface is nodular.
- Non-tender.
- Hard in consistency.
- Upper border of liver dullness in . . . intercostal space in right midclavicular line.
- There is no hepatic bruit.

My differential diagnoses are:

- Hepatoma.
- Secondary deposit in liver.
- Hydatid cyst.
- Polycystic liver.
- Cirrhosis of liver (macronodular).

Q: If it is hydatid cyst, how does the patient present?

A: As follows:

- Usually asymptomatic.
- Mass in right hypochondrium.
- Occasionally jaundice (due to obstruction in bile duct).
- Rarely features of complications such as rupture into the abdominal cavity, pleural cavity or biliary tree may occur. If it ruptures into the biliary tree, there may be jaundice, abdominal pain and fever. If it ruptures into the bronchus, may cause expectoration and spontaneous cure.
- Calcification of cyst occurs in 40% of cases.

N.B.: Features of cyst in other organs:

- *Hydatid cyst in the lung: may be asymptomatic, or infected causing lung abscess.*
- *Hydatid cyst in the brain: may cause seizure.*
- *Hydatid cyst in the kidney: haematuria or lumbar pain.*

Q: What are the complications of hydatid cyst?

A: As follows:

- Pressure effect to the surrounding tissue.
- Rupture (abdominal or pleural cavity, biliary tree), may cause anaphylactic shock.
- Secondary infection.

Q: What are the sites of hydatid cyst?**A:** As follows:

- Liver: 60%, usually right lobe (liver is the first filter).
- Lungs: 30% (it is the second filter).
- Kidneys: 3%.
- Brain: 1%.
- Bone: 1%.
- Any organ (spleen, heart, muscles and biliary tree).

Q: How human is infected by hydatid cyst?

A: Close contact with infected dog or eating undercooked vegetables or drinking water contaminated with faeces of infected dog. Infection commonly occurs during childhood. After ingestion of the eggs, the embryo is liberated from the ovum in the small intestine, enters into the blood stream and is carried to other organs. A slowly growing thick-walled cyst is formed. Further larval stage of the parasite develops inside the cyst.

Q: Who are the definitive and intermediate hosts?**A:** As follows:

- Definitive host: Dogs (common) and other canine animals (fox, wolf and jackal).
- Intermediate host: Sheep (common), pig, cattle, goat and man.

Q: What are the organisms of hydatid cyst?**A:** As follows:

- Echinococcus granulosus of dogs.
- Echinococcus multilocularis (life cycle between fox and vole. Man is infected accidentally).

Q: How dogs are infected?

A: By eating infected meat of sheep, pig, cow. These animals are infected while grazing in the field contaminated with dog's faeces.

Q: What investigations do you suggest?**A:** As follows:

1. CBC (high eosinophils).
2. USG and CT scan: Shows cyst and also daughter cysts within the parent cyst ('floating membranes' in a hydatid cyst can be seen on ultrasound called 'ultrasound water lily sign'. The 'water lily sign' is usually seen in x-ray in pulmonary hydatid disease where ruptured hydatid cyst has daughter cyst floating within the cavity).
3. Serology:
 - CFT (70 to 80% positive).
 - Haemagglutination test (85% positive).
 - Flocculation test.
 - Indirect fluorescent antibody test.
 - Immunoelectrophoresis test (Arc5-test).
 - ELISA (70 to 90% positive).
4. Plain abdomen X-ray (calcification may be seen).
5. Casoni test (non-specific): It is done by intradermal injection of 0.2 mL hydatid fluid in forearm (control with normal saline in other arm. In positive cases, there is formation of wheal with pseudopodia in 20 to 30 minutes, disappears in 1 hour).

Q: How to **treat** hydatid cyst?

A: As follows:

1. Surgical treatment: Cyst should be removed, if possible, after first sterilizing the cyst with alcohol, 2.7% NaCl or 0.5% silver nitrate. Praziquantel 20 mg/kg twice daily for 14 days kills protoscolices perioperatively. Albendazole 15 mg/kg daily in two divided doses 4 days before to 4 weeks after the procedure, helps to reduce the size and prevent recurrence.
2. Medical treatment:
 - Albendazole 15 mg/kg in two divided doses for 12 weeks to 6 months. May be repeated (cures in 30% and symptomatic relief in 50% cases).
 - Mebendazole 400 mg twice daily for 12 weeks to 6 months, may be repeated.
3. PAIR therapy (Puncture, Aspiration, Injection and Re-aspiration): Percutaneous partial aspiration of cyst, followed by injection of scolicidal agent (95% ethanol, hypertonic saline or 0.5% cetrimide) into the cyst, then re-aspiration of cyst contents. Albendazole, 15 mg/kg daily in two divided doses 4 days before to 4 weeks after the procedure or mebendazole may be combined with PAIR.
4. Calcified cyst may be left untreated.

ASCITES

Instruction by the examiner:

- Look at the abdomen, what are your findings?
- Examine or palpate the abdomen and see the relevants.

Presentation of a Case:

- There is generalized distension of abdomen, flanks are full, umbilicus is everted.
- Shifting dullness is present.
- Fluid thrill is present (mention if any).
- No hepatosplenomegaly (may be engorged vein, see the flow).

My diagnosis is **Ascites**.

Q: Why it is ascites?

A: Because there is shifting dullness (also fluid thrill, which is present in tense ascites).

Q: What are the causes of abdominal distension?

A: Fluid, fat, flatus, faeces and foetus (5 F). Others: intra-abdominal mass, retention of urine.

Q: How to confirm ascites clinically?

A: By eliciting shifting dullness, also fluid thrill (present in tense ascites).

Q: What relevants do you like to see in ascites?

A: As follows:

- Stigmata of CLD (page 393).
- Generalized swelling in face, leg, other parts of the body (due to nephrotic syndrome, hypoproteinaemia).
- Engorged neck vein, leg oedema and heart (which are found in CCF and chronic constrictive pericarditis).
- Lymph node (lymphoma, disseminated TB).
- Chest (to see any pleural effusion).

Q: What are the causes of ascites in this case?

A: Mention the causes of that patient in relation to age, also sex:

- Cirrhosis of liver with portal hypertension (commonest cause, in 80% cases).
- Intra-abdominal malignancy with peritoneal metastasis (in elderly).
- Infection (tuberculous or pyogenic peritonitis).
- CCF.
- Others: Hypoproteinaemia due to any cause, Meigs' syndrome (in female).

Q: What are the common causes of ascites?

A: As follows:

- Cirrhosis of liver with portal hypertension.
- Tuberculous peritonitis.
- Intra-abdominal malignancy with peritoneal metastasis (usually ovarian and GIT).



Ascites



Ascites with engorged vein



Ascites in nephrotic syndrome

Q: What is the **single investigation** to detect ascites?

A: Ultrasonography.

Q: What is **ascites**? How much **fluid** is required to detect ascites clinically?

A: It is the pathological accumulation of free fluid in peritoneal cavity. Usually 2 L fluid is necessary to detect clinically (at least 1 L is necessary, even in thin person). Pleural effusion may be present in 10% cases with ascites, usually on the right side, mostly small, occasionally massive and unusual on left side.

N.B. Normally, no or little fluid is present in peritoneal cavity. In female, up to 20 mL may be present, varies with menstruation.

Q: If the patient has **cirrhosis** and **ascites**, what does it **indicate**?

A: Decompensated cirrhosis with portal hypertension (a bad prognostic sign).

Q: What is the **character** of ascitic fluid in CLD?

A: Usually clear, may be straw or light green and transudative.

Q: What **investigations** are done in ascites?

A: As follows (according to suspicion of cause):

1. USG of abdomen (to see liver, spleen, para-aortic lymph nodes, neoplasm, ovary in female to exclude Meigs' syndrome).
2. If CLD is suspected: LFT should be done (see in **CLD**).
3. CBC (high ESR in TB, leucocytosis in pyogenic infection. Pancytopenia with splenomegaly indicates hypersplenism).
4. Chest X-ray (to see TB, cardiomegaly, chronic constrictive pericarditis. May be pleural effusion).

5. Ascitic fluid aspiration for the following tests:
 - Naked eye examination (straw coloured, blood stained, serous and chylous).
 - Gram staining and C/S (in pyogenic infection).
 - Cell count (neutrophil >250 cells/mm³ or WBC >500 cell/mm³ indicates SBP, high lymphocyte in tuberculous peritonitis).
 - Biochemistry (protein and sugar)—high protein in exudative and low protein in transudative. Simultaneous serum albumin to see **serum ascitic albumin gradient** (see below).
 - In tuberculous peritonitis: examine the fluid for ADA, AFB, PCR and mycobacterial C/S.
 - Exfoliative cytology (to see malignant cells).
 - Fluid amylase in acute pancreatitis (>1000 is highly suggestive).
6. Other tests (according to suspicion of causes):
 - For tuberculous peritonitis: MT.
 - Urine for proteinuria and serum total protein, albumin, A:G ratio (in nephrotic syndrome).
 - Endoscopy, colonoscopy according to suspicion.
7. CT scan or MRI (if any growth or mass suspected).
8. Laparoscopy and biopsy in some cases.

Serum-ascites albumin gradient (SAAG): It is the difference of albumin between serum and ascitic fluid (calculated by serum albumin minus ascitic albumin). This gradient correlates directly with portal pressure. It is the single test to differentiate ascites due to portal hypertension from non-portal hypertension.

- If the gradient is >1.1 g/dL, it indicates CLD with portal hypertension.
- If <1.1 , no portal hypertension (Indicates ascites due to non-portal hypertension. It is 97% accurate.)

N.B. Ascites protein <25 g/L and SAAG >1.1 g/dL is usually suggestive of portal hypertension.

READ THE FOLLOWING POINTS IN RELATION TO ASCITES

Q: What are the **complications** of ascites?

A: As follows:

- SBP.
- Hepatorenal syndrome.
- Mesenteric vein thrombosis.
- Herniae (umbilical, femoral, inguinal).
- Hydrothorax.
- Respiratory embarrassment.

Q: What are the **causes** of ascites?

A: As follows:

1. Liver diseases: cirrhosis of liver with portal hypertension (commonest). Other causes are—hepatoma with secondary in peritoneum, Budd–Chiari syndrome.
2. Abdominal: intra-abdominal malignancy with peritoneal metastasis, carcinoma kidney, stomach, colon, ovary.
3. Peritoneal disease: peritonitis (TB or pyogenic) and secondaries in the peritoneum.

4. Cardiovascular: chronic constrictive pericarditis and CCF (in advanced stage).
5. Hypoproteinaemia: nephrotic syndrome, malnutrition and malabsorption.
6. Others:
 - Collagen disease (SLE, PAN).
 - Lymphoma, leukaemia.
 - Meigs' syndrome (characterized by ovarian fibroma, ascites and right sided pleural effusion).
 - Acute pancreatitis.
 - Myxoedema.
 - Chylous ascites.

Ascites may be exudative or transudative:

1. Transudative causes (protein <25 g/L):
 - Cirrhosis of liver with portal hypertension.
 - Nephrotic syndrome.
 - CCF.
 - Meigs' syndrome.
 - Other causes of hypoproteinaemia (malnutrition and malabsorption).
2. Exudative causes (protein >25 g/L):
 - Peritonitis (TB and pyogenic).
 - Malignancy.
 - Collagen disease.
 - Myxoedema.
 - Others: acute pancreatitis, chylous ascites, Budd–Chiari syndrome.

Q: What are the causes of ascites depending on SAAG?

A: As follows:

- A.** High SAAG (>1.1 g/dL), causes are:
 1. Ascitic protein >25 g/L
 - CCF.
 - Chronic constrictive pericarditis.
 - Early Budd–Chiari syndrome.
 - IVC obstruction.
 - Sinusoidal obstruction syndrome.
 2. Ascitic protein <25 g/L
 - Cirrhosis.
 - Late Budd–Chiari syndrome.
 - Massive liver metastasis.
- B.** Low SAAG (<1.1 g/dL), causes are:
 - Nephrotic syndrome.
 - Pancreatitis.
 - Peritoneal carcinomatosis.
 - Tuberculosis.
 - Biliary leak.

Causes of ascites with lymphadenopathy:

- Lymphoma.
- SLE.
- Disseminated TB.
- Disseminated malignancy.
- ALL or CLL.
- CML with blastic crisis.

Causes of ascites with generalized oedema:

- CCF (in advanced stage).
- Nephrotic syndrome.
- Myxoedema.
- Hypoproteinaemia (malnutrition and malabsorption).

Causes of hepatomegaly with ascites:

- Cirrhosis of liver with hepatoma.
- Hepatoma with secondary in the peritoneum.
- Congestive cardiac failure or chronic constrictive pericarditis.
- Lymphoma.
- Disseminated TB.
- Budd–Chiari syndrome.
- Disseminated malignancy (secondary in liver and peritoneum).

Causes of splenomegaly with ascites:

- Cirrhosis of liver with portal hypertension.
- Collagen disease (SLE).
- Lymphoma.
- Leukaemia.
- Disseminated TB.

Causes of hepato-splenomegaly with ascites:

- Cirrhosis of liver with portal hypertension (in PBC, haemochromatosis).
- Collagen disease (SLE).
- Lymphoma.
- Leukaemia (e.g., CML).
- Disseminated TB.

Causes of haemorrhagic ascites:

- Traumatic.
- Malignancy.
- Ruptured ectopic pregnancy.
- Acute haemorrhagic pancreatitis.
- Rupture of spleen.
- Any cause of bleeding disorder.
- Occasionally, tuberculous peritonitis.

Causes of straw coloured ascites:

- Tuberculous peritonitis (common).
- Occasionally, cirrhosis of liver.

Causes of cloudy ascites:

- Pyogenic infection.
- SBP.

Causes of chylous ascites (milky colour, high triglyceride and Sudan black staining of ascitic fluid shows fat cells):

- Trauma.
- Filariasis.
- Tuberculosis.
- Malignancy.

Q: What is refractory ascites? What are the causes? How to treat?

A: Persistence of ascites despite maximum diuretic therapy (up to 400 mg spironolactone and 160 mg furosemide per day) with salt and water restriction, is called refractory ascites. Causes are:

- Poor compliance.
- Severe hypoalbuminaemia.
- Infection (SBP).
- Development of HCC in cirrhosis or secondary causes like metastasis or TB.

Treatment: See the compliance, correction of albumin, paracentesis, TIPSS, LeVeen shunt, also treatment of primary cause.

ASCITES (DISCUSSION ABOUT TUBERCULOUS PERITONITIS)

Instruction by the examiner:

- Look at the abdomen, what are your findings? Or, examine or palpate the abdomen and see the relevants.

Presentation of a Case:

Present as described is ascites.

My differential diagnoses are:

- See in ascites (mention the cause according to age of the patient).

Q: How to diagnose tuberculous peritonitis?

A: As follows:

1. History:

- History of pulmonary tuberculosis.
- General features of tuberculosis such as low grade fever with evening rise, weight loss, sweating.
- Abdominal pain, diarrhoea or features of intestinal obstruction.

2. Physical examination:

- Patient is ill looking and emaciated.
- Abdomen is doughy.
- Mass in right iliac fossa (ileocaecal TB).

3. Investigations:

- CBC, ESR.
- MT (positive in 50% cases).
- Chest X-ray (may be primary focus in 50% cases).
- USG of abdomen, CT scan in some cases.
- Ascitic fluid study:
 - Straw colour.
 - High protein >25 g/L (exudative), low glucose.
 - Cell count shows high lymphocyte.
 - Adenosine deaminase (ADA) is high.
 - AFB are rarely found. Mycobacteria C/S may be positive in 50% cases.
 - PCR of ascitic fluid.
- Laparoscopy: Tubercle may be seen over the peritoneal and omental surface (biopsy should be taken).

Q: What is the commonest site of abdominal tuberculosis?

A: Ileo-caecal region (peritoneum is the second common site).



Huge ascites

Q: What are the **types** of tuberculous peritonitis?

A: 3 subgroups:

- Wet type: In such case, ascitic fluid protein is >20 gm/L, tubercle bacilli are rarely found.
- Dry type: In such case, patient presents with subacute intestinal obstruction, which is due to tubercular small bowel adhesion.
- Fibrous type: In such case, patient presents with abdominal pain, distension and ill-defined irregular tender abdominal mass.

Q: What is the **feeling** of abdomen on palpation in tuberculous peritonitis?

A: Doughy feeling.

Q: How to treat?

A: As follows:

- Standard anti-TB drugs for at least 1 year.
- Surgery in some cases (if fistula or obstruction).
- Symptomatic treatment for pain and diarrhoea.
- Prednisolone in some cases.

CHRONIC LIVER DISEASE OR CIRRHOSIS OF LIVER

Instruction by the examiner:

- Look at the abdomen, what are your findings?
- Examine or palpate the abdomen and see the relevants.

(May be isolated splenomegaly or ascites with splenomegaly, hepatomegaly or hepatosplenomegaly or ascites)

Presentation of a Case:

- There is generalized distension of abdomen, flanks are full and umbilicus is everted.
- Shifting dullness is present.
- Fluid thrill is present (mention if any).
- Spleen is enlarged, 2 cm from the left costal margin in anterior axillary line towards the right iliac fossa.

My diagnosis is **ascites with splenomegaly**, which is more likely due to cirrhosis of liver with portal hypertension.

Q: What are the **CLD**?

A: Cirrhosis of the liver, also chronic hepatitis.

Q: What are the causes of **splenomegaly with ascites**?

A: As follows:

- Cirrhosis of liver with portal hypertension.
- Collagen disease (SLE).
- Lymphoma.
- Leukaemia.
- Disseminated TB.

Q: What **else** do you like to see?

A: I want to see the stigmata of CLD.

Q: What are the **stigmata** or **signs** of CLD?

A: As follows:

1. In the face:
 - Parotid enlargement (bilateral).
 - Xanthelasma (common in PBC).
 - Spider angioma (also in neck, arm, forearm, hand and any part above the nipple line).
 - Pigmentation.
 - Hepatic facies.
 - Jaundice.
 - Cyanosis (in hepato-pulmonary syndrome).

2. In hands:
 - Palmar erythema (also called liver palm).
 - Dupuytren's contracture.
 - Leuconychia.
 - Clubbing.
 - Flapping tremor.
 - Others: scratch marks, spider angioma, xanthoma, pigmentation, jaundice and cyanosis.
3. Chest:
 - Gynaecomastia (also spider angioma).
 - Less hair in chest or body, scanty axillary (also pubic hair).
 - Engorged veins in chest and also abdomen (due to portal hypertension).
4. Others:
 - Abdomen: ascites, splenomegaly, engorged veins and caput medusae.
 - Testis (small and atrophied).
 - Generalized pigmentation (any CLD can cause pigmentation, but commonly in haemochromatosis and primary biliary cirrhosis).
 - Purpura and ecchymosis.

Q: What specific findings will you see in CLD in a young patient?

A: As follows:

- In eye: **Kayser–Fleischer** (KF) ring for Wilson's disease.
- In lung: signs of emphysema may be present in α_1 -antitrypsin deficiency.

Q: What are the signs in alcoholic cirrhosis or alcoholic liver disease?

A: As follows:

- Bilateral parotid enlargement.
- Florid spider angioma.
- Dupuytren's contracture.
- Gynaecomastia.
- Testicular atrophy with loss of body hair.

Q: What are the causes of CLD with hepatomegaly?

A: In CLD, liver is usually small. Hepatomegaly may be found in:

- Haemochromatosis.
- Primary biliary cirrhosis.
- Alcoholic liver disease (in early stage).

Q: What is chronic liver disease (CLD) and chronic liver failure?

A: As follows:

- CLD is defined as liver disease for 6 months or longer.
- Chronic liver failure means functional capacity of liver cannot be maintained and is characterized by encephalopathy and/or ascites. When chronic liver failure occurs, it is called decompensated liver disease.

Q: What is cirrhosis of liver? What are the types?

A: Cirrhosis of liver is a chronic diffuse liver disease characterized by destruction of liver cells with fibrosis, distortion of normal liver architecture and nodular regeneration due to proliferation of surviving hepatocytes. **3 types** of cirrhosis are:

- Micronodular: Regenerative nodule is small, 1 mm size, involving every lobule, also called Laennec cirrhosis, common in alcoholics.
- Macronodular: Large nodules, common in post-necrotic cirrhosis, found in HBV.
- Rarely, mixed type (micronodular and macronodular).

Q: What are the signs of portal hypertension?

A: As follows:

- Splenomegaly (single definite sign, mild in adult but marked splenomegaly in childhood and adolescent). Hypersplenism may occur (CBC shows pancytopenia).
- Ascites.
- Collateral circulation, oesophageal varices, haemorrhoid and venous hum (between xiphisternum and umbilicus called Cruveilhier–Baumgarten syndrome), Caput Medusae.
- Porto-systemic encephalopathy.
- Endoscopy shows oesophageal varices.

N.B. Remember the following points:

- *Normal portal pressure, 2 to 5 mmHg. In portal hypertension >7 mmHg. If >12 mmHg, symptoms and complications may develop.*
- *Portal vein is formed by fusion of superior mesenteric vein and splenic vein.*
- *In adults, cirrhosis of liver is the common cause of portal hypertension.*
- *In children, extrahepatic portal vein obstruction is the common cause.*

Q: What are the causes of cirrhosis of liver?

A: As follows:

- Chronic viral hepatitis (B or C, or B and D).
- Chronic alcoholism.
- Non-alcoholic fatty liver disease (NAFLD).
- Immunological (autoimmune liver disease and primary sclerosing cholangitis).
- Biliary: primary biliary cirrhosis, secondary biliary cirrhosis and cystic fibrosis.
- Genetic (haemochromatosis, Wilson's disease and α_1 -antitrypsin deficiency).
- Budd–Chiari syndrome.
- Drugs: Methotrexate, Amiodarone, Phenytoin.
- Idiopathic or cryptogenic (15%).

Q: What are the commonest causes of cirrhosis of liver?

A: Viral infection (B and C), alcohol, NAFLD. In young patient, Wilson's disease.

Q: What are the signs of decompensated cirrhosis?**A:** As follows:

- Ascites (SBP, hepatorenal failure).
- Increasing jaundice.
- Hepatic encephalopathy.
- Portal hypertension with variceal bleeding.
- Worsening liver function (prolonged PT and low albumin).

Q: What are the complications of cirrhosis of liver?**A:** As follows:

- Portal hypertension with rupture of oesophageal varices (haematemesis and melaena).
- Porto-systemic encephalopathy (hepatic precoma) and hepatic coma.
- Hepatorenal syndrome.
- Hepatopulmonary syndrome.
- Spontaneous bacterial peritonitis (SBP).
- Hepatoma.

Q: If patient of CLD with ascites complains of fever and abdominal pain, what is the likely diagnosis?**A:** Spontaneous bacterial peritonitis (other causes of fever in CLD with ascites are secondary infection, hepatoma and excess pyrogen accumulation).**Q: If patient with CLD deteriorates, what are the possibilities?****A:** As follows:

- Spontaneous bacterial peritonitis.
- Hepatocellular carcinoma.
- Hepatic encephalopathy.

Q: What are the clinical features of CLD?**A:** May be asymptomatic in many cases. Diagnosed incidentally during USG or after laparotomy.

Other features are:

- General features: Weakness, fatigue, weight loss, low grade fever.
- GIT features: Anorexia, nausea, vomiting, abdominal discomfort, distension (due to ascites).
- Features of hepatocellular insufficiency: jaundice, encephalopathy, splenomegaly.
- Features of portal hypertension: ascites, variceal bleeding (haematemesis, melaena), splenomegaly.
- Endocrine abnormalities: loss of libido, hair loss. In male: gynaecomastia, testicular atrophy, impotence. In female: breast atrophy, irregular menses, amenorrhoea.
- Coagulation abnormality: bruising, purpura, epistaxis.
- Signs are: **(see in the stigmata of liver disease).**

Q: What are the bad prognostic signs of CLD?**A:** As follows:**1. Clinical:**

- Increasing jaundice.
- Ascites.
- Porto-systemic encephalopathy.

2. Laboratory:

- Increasing bilirubin.
- Falling plasma albumin <30 g/L.
- Prothrombin time: Prolonged.
- Sodium <120 mmol/L (not due to diuretic).

Q: What is the mechanism of ascites in cirrhosis of liver?

A: It is mainly due to sodium and water retention. Multiple factors are involved, such as:

1. Splanchnic vasodilatation is the main factor, mediated by mainly nitric oxide, released when portal hypertension causes shunting of blood into systemic circulation. Due to splanchnic vasodilatation, systemic arterial pressure falls, which activates renin–angiotensin mechanism with secondary aldosteronism, increased sympathetic activity, increased ANP and altered activity of kallikrein–kinin system. All these produce salt and water retention.
2. Other factors are:
 - Increased intestinal capillary permeability.
 - Increased hepatic lymph production, which accumulates into the peritoneal cavity.
 - Low albumin causes low plasma osmotic pressure, causes extravasation of fluid.
 - Failure to metabolize vasopressin by the liver that causes further retention of fluid.

Q: How to treat ascites in cirrhosis of liver?

A: As follows:

1. Bed rest. It improves renal flow (in horizontal position) and increases diuresis.
2. Sodium and water restriction:
 - Sodium 88 mmol/day (no added salt), in severe case 40 mmol/day.
 - Water 0.5 to 1 L/day (fluid restriction is not necessary, unless sodium is <125 mmol/L).
 - Avoid salt-containing and salt-retaining diets and drugs (NSAIDs, steroid and antacid).
3. Monitor weight, abdominal girth and urinary output daily. Weight loss should be 0.5 to 1 kg/day (fluid loss should not be more than 1 L daily).
4. Measure serum electrolyte and creatinine.
5. Few patients will respond to the above therapy.

If no response in 4 days with above therapy:

- Diuretic: spironolactone 100 to 400 mg/day is given. If no response, frusemide 40 to 160 is added. If no response with spironolactone 400 mg plus frusemide 160 mg daily, it is considered as refractory ascites. Prolonged use of spironolactone can cause painful gynaecomastia and hyperkalaemia. Eplerenone 25 mg once daily may be a suitable alternative (does not cause gynaecomastia).

If no response or refractory ascites:

- Ensure that patient is not taking any salt or salt-containing diet or drugs.
- If serum protein (mainly albumin) is low, diuretic is not effective. IV salt poor albumin followed by IV frusemide may be given. IV dextran may be tried.

If still no response (refractory or resistant ascites), paracentesis may be necessary:

- It is indicated in huge ascites with cardiorespiratory embarrassment or resistant ascites.
- 3 to 5 Litres of fluid can be removed. It is safe provided circulation is maintained (no fear of hepatic encephalopathy, thought previously). After paracentesis, IV albumin (6 to 8 gm/L of ascitic fluid removed, usually 100 ml of 20% human albumin for every 3 L of ascitic fluid drained). Plasma expander such as dextran (8 g/L of ascitic fluid removed) or haemaccel (125 mL/L of ascitic fluid removed) may be used.

Other modes of treatment (in refractory or resistant ascites):

- LeVeen shunt (peritoneo-venous): A catheter is used with one-way valve to communicate between peritoneal cavity and internal jugular vein, which allows ascitic fluid to pass directly into the systemic circulation (rarely done now a days). Its main complications are infection, SVC thrombosis, pulmonary oedema, bleeding from oesophageal varices and DIC.
- TIPSS (transjugular intrahepatic porto-systemic stent shunt): A stent is placed between portal vein and hepatic vein in liver to make porto-systemic shunt, which is carried out under radiological control via internal jugular vein. It is mainly used to reduce portal pressure and also variceal bleeding. It relieves resistant ascites, also frequency of paracentesis and diuretic doses are reduced. It can be done provided reasonable liver function without encephalopathy and minimal disturbance of renal function (TIPSS is ineffective with intrinsic renal disease). Hepatic encephalopathy may occur following TIPSS. This can be managed by reducing the shunt diameter.
- Porto-systemic shunt surgery: Portocaval or splenorenal shunt. Rarely done, may cause encephalopathy.
- Liver transplantation may be considered, if all measures fail.

Q: Will you prefer paracentesis or TIPSS in refractory ascites?

A: TIPSS is preferable than repeated paracentesis, as large volume of fluid and protein are lost in paracentesis. TIPSS can improve survival also.

Q: What are the complications of ascites in CLD?

A: SBP and hepatorenal syndrome.

Q: What is spontaneous bacterial peritonitis (SBP)?

A: It means bacterial infection in peritoneum in a patient with cirrhosis of liver with ascites in the absence of any apparently primary source of infection. SBP may develop in 8% cases (up to 18%). It is usually by single organism (monomicrobial). Source of infection cannot be determined usually (so it is called spontaneous), suspected in any patient with ascites who presents with fever with deterioration of general condition.

Causes or mechanism of SBP: Infective organisms gain access to peritoneum by haematogenous route or mesenteric lymphatics. Most organisms are of enteric origin, mainly *Escherichia coli*. Other organisms are *Klebsiella*, *Haemophilus*, *Enterococcus*, other enteric Gram-negative organisms, rarely pneumococcus and streptococcus. Anaerobic bacteria are not usually associated with SBP.

Clinical features: Patient with cirrhosis and ascites may present with sudden abdominal pain, fever, increasing ascites, not responding to diuretic. Abdominal signs are rebound tenderness, absent bowel sounds. Signs may be mild or absent in one-third patients. In these patients, hepatic encephalopathy and fever are the main features.

Ascitic fluid in SBP shows the following:

- Fluid looks cloudy (exudative is with high protein and low sugar).
- Neutrophil counts of fluid $>250/\text{mm}^3$.
- Ascitic fluid C/S: gives the highest yield of organisms (C/S may be negative also).

Treatment of SBP: Pending the result of C/S, if neutrophil in ascitic fluid is high, treatment should be started immediately as follows:

- Broad-spectrum antibiotics: Cefotaxime 2 g 8 to 12 hourly for at least 5 days or piperacillin/tazobactam.
- Ceftriaxone **plus** amoxiclav is an alternative.
- Intravenous human albumin solution may reduce mortality.

Prognosis of SBP: Mortality is 10 to 15%. SBP is an indication for referral to liver transplantation centre.

Prevention of SBP: Recurrence is common in 70% case within 1 year. This can be prevented by norfloxacin 400 mg daily or ciprofloxacin 500 mg once or twice daily or cotrimoxazole (1 double-strength tablet, 5 days/week). In any patient with acute variceal bleeding, risk of bacterial peritonitis may be reduced by giving injection ceftriaxone 1 g daily or oral norfloxacin. Also, patient with high-risk group in cirrhosis (low albumin, increased PT, low ascitic fluid albumin), norfloxacin may be used to prevent bacterial peritonitis. Non-selective β -blockers should be stopped following diagnosis of SBP, as there is increased risk of renal impairment. Primary prophylaxis of SBP in patients with ascites protein <10 g/L or severe liver disease may prevent hepatorenal syndrome and improve survival.

N.B. Occasionally, there may be secondary bacterial infection other than SBP. To differentiate from SBP, the following features in ascitic fluid may suggest secondary bacterial infection:

- Neutrophil $>10,000$ (very high).
- Total protein: Very high (>1 g/dL is against SBP, highly suggestive of secondary bacterial infection).
- Glucose <50 mg%.
- Ascitic LDH $>$ serum LDH.
- Presence of multiple organisms in culture.

Q: What investigations should be done in CLD?

A: As follows:

1. LFT (total protein, A:G ratio and prothrombin time are the two **most** important tests for CLD. Others are serum bilirubin, SGPT and alkaline phosphatase).
2. USG of whole abdomen (in cirrhosis, liver may be small, shrunken, coarse and high echogenic texture, with splenomegaly, ascites and dilated portal vein).
3. Viral markers for HBV (HBsAg, HBeAg, anti-HBc) and for HCV (anti-HCV).
4. Proctoscopy (to see haemorrhoid).
5. Endoscopy (to see oesophageal varices).
6. CT scan of hepatobiliary system may be done.
7. Liver biopsy under USG control (confirmatory).
8. If CLD is due to other cause, investigation should be done accordingly, such as:
 - In haemochromatosis: Serum iron, TIBC and ferritin.
 - In PBC: Antimitochondrial antibody and other autoantibodies.
 - In younger age, if Wilson's disease is suspected: Serum copper, ceruloplasmin and urinary copper. In α_1 -antitrypsin deficiency: Serum α_1 -antitrypsin (which may be associated with liver disease and pulmonary emphysema, particularly in smokers).
9. Test for ascitic fluid (cytology, biochemistry, SAAG): see in ascites.
10. Other routine investigations:
 - CBC, ESR.
 - Serum urea and creatinine, electrolytes, blood sugar.

Q: What investigations are done to see the **severity** of liver disease?

A: As follows:

- Serum albumin: If <28 gm/L, outlook is poor.
- Prothrombin time: Prolong PT indicates severe liver disease.
- Serum electrolytes: Low sodium indicates severe liver disease due to defect in free water clearance.
- Serum creatinine: High creatinine >130 $\mu\text{mol/L}$ is a marker of worse prognosis.

READ THE FOLLOWING TOPICS IN RELATION TO CLD

Q: What is **hepatorenal syndrome**?

A: Hepatorenal syndrome is a form of functional renal failure without renal pathology in a patient with advanced cirrhosis or acute liver failure. It occurs in 10% cases and is of two **types**:

- Type 1: characterized by progressive oliguria with rapid rise of serum creatinine. No proteinuria, urine sodium excretion is low (<10 mmol/day) and urine/plasma osmolality ratio is >1.5 . Prognosis is poor. Without treatment, median survival is <1 month.
- Type 2: occurs in refractory ascites, characterized by moderate rise of S. creatinine. Prognosis is better.

Mechanism of hepatorenal syndrome: Initially there is vasodilatation possibly due to nitric oxide, which causes hypotension. Also there is high plasma renin, aldosterone, nor-epinephrine and vasopressin, causes vasoconstriction of renal vessels and increases pre-glomerular vascular resistance. There is reduced glomerular filtration rate (GFR) with sodium and water retention. Other mediators like eicosanoids may also be involved.

Renal failure is functional and tubular function is intact. Hepatorenal syndrome may be precipitated by excess diuretic therapy, NSAIDs, diarrhoea or paracentesis and infection, especially spontaneous bacterial peritonitis.

Treatment:

- Diuretic should be stopped.
- Hypovolaemia should be corrected, preferably with albumin.
- Terlipressin or noradrenaline with intravenous albumin may be used. Octreotide may be used also.
- Liver transplantation is the best option.
- Haemodialysis should not be used routinely, because it does not improve the outcome.

Q: What is **hepatopulmonary syndrome**?

A: Hepatopulmonary syndrome is defined as hypoxaemia occurring in a patient with advanced liver disease. PaO_2 is <9.3 kPa or 70 mmHg. It is due to intrapulmonary vascular dilatation with no evidence of primary pulmonary disease. Hypoxia is due to intrapulmonary AV communication. The patient has features of cirrhosis with clubbing, spider angioma and cyanosis. Most patients have no respiratory symptoms. But with more severe disease, the patient is dyspnoeic on standing with characteristic reduction of arterial oxygen saturation.

Transthoracic echo shows intrapulmonary shunting (probably due to excess nitric oxide production). Arterial gas analysis shows low PaO_2 . HRCT is helpful to detect dilated pulmonary vessels.

Liver transplantation is indicated in hepatopulmonary syndrome. Features improve after liver transplantation. But severe hypoxaemia ($\text{PaO}_2 < 6.7$ kPa or 50 mm Hg) is associated with increased operative risk.

Q: What is portopulmonary hypertension?

A: It is defined as pulmonary hypertension and cirrhosis of the liver with portal hypertension. There is increased pulmonary vascular resistance with normal pulmonary artery wedge pressure, found in 1 to 2% cases of cirrhosis. It is caused by vasoconstriction and obliteration of pulmonary artery due to circulating vasoconstrictors, particularly endothelin-1. This leads to breathlessness and fatigue. It may respond to medical therapy (e.g., IV epoprostenol or oral bosentan and sildenafil). Liver transplantation is contraindicated in severe pulmonary hypertension.

PORTO-SYSTEMIC ANASTOMOSIS

Sites are:

1. Lower end of oesophagus:
 - Portal: Oesophageal tributaries of left gastric vein communicate with
 - Systemic: Oesophageal tributaries of azygos veins.
2. Lower end of rectum and anal canal:
 - Portal: superior rectal vein communicates with
 - Systemic: middle and inferior rectal veins.
3. Paraumbilical: (called Caput Medusae)
 - Paraumbilical vein (portal) communicates with systemic veins in superficial epigastric vein.
4. Bare area of liver (intra-hepatic):
 - Portal: Portal radicles of liver communicates with
 - Systemic: diaphragmatic veins by a number of small veins, called accessory portal system of Sappey.
5. Retroperitoneal site:
 - Portal: splenic and colic veins communicate with
 - Systemic: left renal veins and other tributaries of inferior vena cava by small veins called veins of Retzius.
6. Fissure for ligamentum venosum: rarely, persistent ductus venosus establishes direct portacaval anastomosis

(In foetal life, left branch of portal vein at the porta hepatis communicates with IVC via ductus venosus. After birth, ductus venosus is fibrosed to form ligamentum venosum).

SPIDER ANGIOMA (SPIDER NAEVI)

Def: Spider angioma is a type of telangiectasis which consists of central arteriole from which numerous capillaries radiate, looks like spider legs. Size varies from pinhead to 1 to 2 mm (sometimes 1 to 2 cm). These are found along the area of superior vena cava, common in neck, face, chest and dorsum of hand, above the nipple lines, cause of which is unknown. Blanchs on pressure with rapid filling on release of pressure, may pulsate if large. Better seen with glass slide or pinhead. It is a sign of hepatocellular failure.

Causes of spider angioma:

1. Physiological:

- Rarely present in normal people (2%), 1 to 2 in number, common in children. Usually pathological if >3 , especially in male than female.
- Pregnancy (usually in the 3rd trimester, disappears after 2 months of delivery).

2. Pathological:

- CLD, commonly alcoholic cirrhosis (disappears with improvement of liver function. Appearance of new spider indicates deterioration of liver function).
- Viral hepatitis (transient).
- Oestrogen therapy and oestrogen containing oral contraceptive pill.
- Rarely, in rheumatoid arthritis, thyrotoxicosis.



Spider angioma in shoulder



Spider angioma in hand



Spider angioma in nose



Spider angioma in face

Mechanism of spider angioma:

- Due to hyperdynamic circulation.
- Excess oestrogen level (due to reduced metabolism by the liver).

Differential diagnoses of spider angioma:

- Purpura (spontaneous bleeding into skin and mucous membrane, does not blanch on pressure, there is progressive colour change).
- Hereditary haemorrhagic telangiectasia.
- Campbell de Morgan's spots (common in elderly, 1 to 2 mm in diameter, elevated from skin surface, nodular, does not blanch on pressure).
- Venous stars.
- Mosquito bite.
- Rose spot (in enteric fever).

VENOUS STARS

Def: Venous stars are star-like lesions, 2 to 3 cm in size, that occur on dorsum of foot, leg, back and lower chest, on sites overlying the main tributary to a large vein.

It is caused by elevated venous pressure, does not blanch on pressure and blood flow is from periphery to the centre of lesion (opposite to spider angioma).



Venous star

PALMAR ERYTHEMA (LIVER PALM)

Def: It is the redness of palm involving the thenar, hypothenar eminence, also pulp of fingers. Blanches on pressure. With glass slide, flushes synchronously with pulse. May be found in soles of feet, called plantar erythema.

Causes of palmar erythema:

1. Physiological:
 - Normal people, may be familial.
 - Pregnancy (up to 30%).
 - Idiopathic.
2. Pathological:
 - CLD (commonly alcoholic).
 - Thyrotoxicosis.
 - Polycythaemia.
 - Prolonged rheumatoid arthritis.
 - Leukaemia.
 - Febrile illness.

Mechanism of palmar erythema in CLD:

- Hyperdynamic circulation.
- Probably, high oestrogen. Because circulating levels of oestrogen increase in both cirrhosis and pregnancy, oestrogen is thought to be the cause for the increased vascularity.
- More recently, nitric oxide has been implicated in the pathogenesis of palmar erythema.



Palmar erythema



Palmar erythema



Plantar erythema

Investigations: These will depend on the underlying condition(s) suggested by the overall clinical picture. Idiopathic palmar erythema should be a diagnosis of exclusion.

CLUBBING IN CLD

Clubbing is found in any CLD (up to 1/3rd of patients with cirrhosis of liver), common in primary biliary cirrhosis.

Mechanism in CLD: It is usually due to hyperdynamic circulation, may also be due to hepato-pulmonary syndrome, related to arterio-venous shunt in the lung resulting in arterial oxygen desaturation.

LEUKONYCHIA

In CLD, leukonychia is due to hypoalbuminaemia. Fingers and toes both are involved. It is also a sign of hepatocellular failure. Transverse white lines may also be seen in hypoalbuminaemia associated with liver cirrhosis.

DUPUYTREN'S CONTRACTURE

It is found in CLD. For details, see in chapter 1.

FLAPPING TREMOR (ASTERIXIS)

Def: It is characterized by irregular, flexion–extension movement of wrist and metacarpo-phalangeal (MCP) joints, accompanied by lateral movement or abduction–adduction of fingers. It is called flapping, because of resemblance to a bird flapping its wings.

It is elicited by asking the patient to stretch out arms in front, separate the fingers, dorsiflexion of wrist with fixed forearm by the examiner's hand. The term derives from the Greek *a*, 'not' and *stēixis*, 'fixed position'.

N.B.: It looks like goodbye (previously it was thought that condition is so serious that patient is going to die).

Features of flapping tremor:

- It is absent at rest, produced by intentional movement, maximum at sustained posture.
- Usually bilateral, not necessarily synchronous on each side.
- Disappears during coma (hepatic coma).
- Occasionally arms, face, neck, tongue, jaw and eyelids are involved.

Causes of Flapping Tremor:

- Hepatic encephalopathy (commonest cause).
- Severe cardiac failure.
- Respiratory failure (due to CO₂ retention in COPD).
- Renal failure (Azotaemia).
- Others causes (rare): CVD, drug toxicity (phenytoin and barbiturate), acute focal parietal or thalamic lesion (vascular), hypoglycaemia, hypokalaemia, Wilson's disease.

Mechanism of flapping tremor in CLD:

- It is due to impaired inflow of joint position sense and other afferent information to the brainstem reticular formation, resulting in rhythmical lapse of postural muscle tone.
- Also, as the relay system between cerebrum and cerebellum is under toxic effect of neurotoxin, cerebellum fails to maintain the co-ordination. The repetition of the process causes flapping tremor.

Q: What is foetor hepaticus?

A: It is a bad smell (slightly faecal) of breath, like that of dead mouse. It is due to methyl mercaptan, exhaled in breath, derived from amino acid methionine, which is not deaminated by the diseased liver. Methyl mercaptan is of intestinal origin (reduced by defaecation or use of antibiotics). Presence of foetor hepaticus indicates severe hepatocellular failure with collateral circulation.

Q: What are the causes of bad breath (halitosis)?

A: As follows:

- Hepatic precoma (foetor hepaticus).
- Diabetic ketoacidosis (sweetish due to ketone body).
- Renal failure (fishy ammoniacal).
- Lung abscess with anaerobic infection (may be foetid).
- Others: faulty oral hygiene and alcoholism.

Q: Why itching in liver disease?

A: Itching is common in primary biliary cirrhosis and obstructive jaundice. Actual cause is unknown, probably due to upregulation of opioid receptors and increased levels of endogenous opioids.

Q: What are the vitamin K-dependent coagulation factors?

A: Factors II, VII, IX and X (Vit K is needed in the post translational modification of these factors).

Q: In which liver disease, vitamin K therapy is helpful?

A: Obstructive jaundice, as bile salt is necessary for absorption of vitamin K. Less or not helpful in parenchymal liver disease, as vitamin K is not used or less used by the diseased liver.

N.B. PT depends on factors I, II, V, VII and X. In CLD, PT is prolonged when these factors fall below 30%.

PORTO-SYSTEMIC ENCEPHALOPATHY (DISCUSSION ABOUT PSE OR HEPATIC PRECOMA)

Definition: Portosystemic encephalopathy is a state of neuropsychiatric syndrome due to biochemical disturbance of brain function caused by chronic liver disease. It may progress from confusion to coma.

Liver failure and portosystemic shunting are two important factors for PSE. It is reversible, does not cause marked pathological change in brain and may cause cerebral oedema in advanced stage.

PSE may occur due to:

- Cirrhosis with portal hypertension (commonest).
- Also after surgery such as portocaval or TIPS shunt.

Mechanism of PSE: It is due to involvement of brain by nitrogenous substances of gut origin. Normally, these substances are metabolized by healthy liver. In diseased liver, these are not metabolized and enter into the brain through portosystemic shunt.

Nitrogenous substances are:

- Ammonia (due to breakdown of protein by intestinal bacteria).
- γ -Aminobutyric acid (GABA).
- Amino acid, mercaptan, fatty acids and octopamine, all of which act as false neurotransmitters.

Factors precipitating PSE (by increasing the availability of nitrogenous substance):

- High dietary protein.
- Gastrointestinal bleeding.
- Constipation.
- Drugs (sedative, antidepressants and diuretics).
- Infection.
- Spontaneous bacterial peritonitis.
- Fluid and electrolyte imbalance due to diuretics or paracentesis.
- Trauma.
- Paracentesis.
- Surgery (shunt surgery, TIPSS or other surgery).
- Development of hepatocellular carcinoma.

Clinical features of PSE (remember mnemonic **DPIST-F**):

- **D: Disturbance** of consciousness (confusion, disorientation, drowsiness, delirium, stupor and later coma).
- **Disorder** of sleep (hypersomnia, inversion of sleep rhythm).
- **P: Personality** change (childish behaviour, abnormal behaviour, apathy, irritability).
- **I: Intellectual** deterioration, from simple mathematical calculation to organic mental function. Earliest is constructional apraxia (**see below**).
- **S: Speech** disturbance (slow, slurred, monotonous and dysphasia) and **sleep** inversion (daytime sleeping).
- **T: Tremor** (flapping tremor).
- **F: Foetor** hepaticus (sweet musty odour in breath).

Other features are:

- Convulsion, exaggerated reflex, extensor plantar response and clonus.
- Rarely, chronic hepatic encephalopathy may be associated with cerebellar dysfunction, Parkinsonism, spastic paraplegia and dementia.

Q: What are the differential diagnoses of PSE?

A: As follows:

- Intracranial bleeding (subdural, extradural haematoma).
- Drug or alcohol intoxication.
- Delirium tremens (alcohol withdrawal).
- Hypoglycaemia.
- Wernicke's encephalopathy.
- Primary psychiatric disorder.
- Neurological Wilson's disease.
- Post-ictal state.

Q: How to diagnose PSE in early stage?

A: By EEG, which shows diffuse slowing in frequency of normal range (8 to 13 Hz) to δ -range (1.5 to 3 Hz). However, diagnosis is mostly clinical.

Q: How to treat PSE?

A: As follows:

- Precipitating factors should be avoided (drugs, constipation, electrolyte imbalance, bleeding).
- **No** sedative and **no** diuretic. No protein restriction is recommended.
- Nutrition: Glucose (300 to 400 g/day) orally. If the patient cannot take by mouth, IV should be given.
- Lactulose: 15 to 30 mL 8 hourly (bowel should move at least twice daily).
- If the patient is unable to take lactulose by mouth, it can be given per rectally (300 mL lactulose in 700 mL saline or lactitol as retention enema).
- Bowel wash (enema should be given if no response to lactulose).
- Gut sterilizer: Metronidazole (200 mg 8 hourly). Rifaximin 550 mg three times daily orally (not absorbed, acts by reducing bacterial content of bowel).
- Correction of electrolyte imbalance (especially hypokalaemia).
- Control of infection by antibiotic.
- Chronic or refractory hepatic encephalopathy is an indication for liver transplantation.
- Other treatment: Zinc deficiency should be corrected, if present.
- If the patient is agitated: Oxazepam (10 to 30 mg) may be given by mouth.
- Other therapy: flumazenil, a benzodiazepine receptor antagonist (may help in some cases).

Q: What is the mode of action of lactulose?

A: Lactulose is a non-absorbable disaccharide, reaches the colon intact, metabolized by colonic bacteria to lactic acid. It acts in the following way:

- Osmotic laxative.
- Lactic acid reduces pH of colonic contents, inhibits ammonia producing colonic bacteria and reduces ammonia absorption by converting ammonia to ammonium, which is not absorbed.
- Promotes incorporation of nitrogen into bacteria.

Q: What is fulminating hepatic failure? What are the types?

A: It is a clinical syndrome of encephalopathy characterized by confusion, stupor and coma, resulting from sudden severe impairment of hepatic function, occurring within 8 weeks of onset in the absence of pre-existing liver disease. It is also called acute liver failure. 3 types:

- Hyperacute (<7 days),
- Acute (within 8 to 28 days) or
- Subacute (29 days to 12 weeks) between the onset of jaundice and encephalopathy.

Q: What are the causes of fulminating hepatic failure?

A: As follows:

- Two **commonest causes** are viral hepatitis (commonly B and E, rarely A) and paracetamol toxicity.
- Other causes—acute fatty liver in pregnancy, Wilson's disease, following shock and rarely extensive malignancy of liver.

Q: What are the clinical features of fulminating hepatic failure?

A: Clinical features are similar to PSE. Other features are:

1. Patient is restless with aggressive outburst.
2. Jaundice, may be deep.
3. Features of cerebral oedema due to raised intracranial pressure, such as:
 - Hyperventilation.
 - Profuse sweating.
 - Pupil—unequal or abnormally reacting fixed pupil.
 - Local or general myoclonus, focal fit, decerebrate posture.
 - Rarely papilloedema.

Q: How to treat fulminating hepatic failure?

A: Treatment is also similar to PSE. Other treatments are:

- If signs of raised ICP—20% mannitol 1 g/kg body weight IV. It may be repeated.
- If coagulopathy or bleeding—IV vitamin K, fresh blood or fresh frozen plasma, platelet concentrate.
- PPI to prevent gastrointestinal bleeding.
- Liver transplantation may be considered.

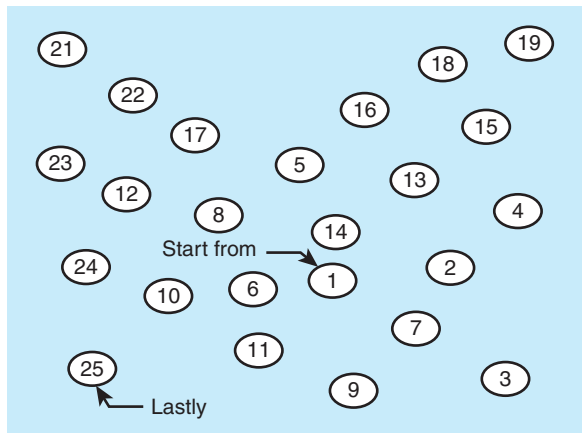
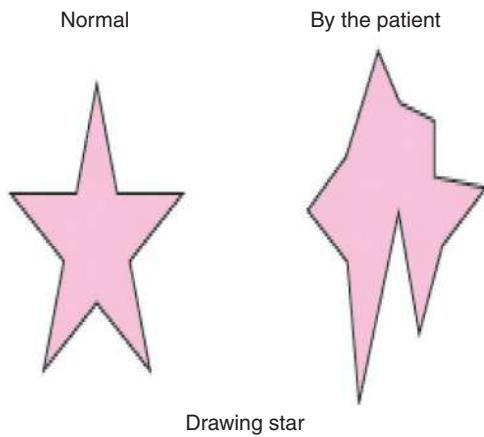
Q: What is constructional apraxia?

A: Constructional apraxia means inability to perform a known act in the absence of any motor or sensory disturbance.

Q: How to test for constructional apraxia?

A: It is tested in the following way (the patient is unable to do so):

- Ask the patient to draw a star.
- Writing disturbance (unable to write or disturbance in writing).
- Ask the patient to make triangle with 3 match sticks.
- Ask to lighten the cigarette by match stick.
- Reitan trail making test (it is the ability to join or connect the numbers with a pen in a certain fixed time). It becomes prolonged in PSE.



From 1 to 25 numbered circles can be joined within 30 second normally. More time is required in PSE

HEPATOMEGALY (DISCUSSION ABOUT PRIMARY BILIARY CIRRHOSIS)

Instruction by the examiner:

- Look at the abdomen, what are your findings?
- Examine or palpate the abdomen and see the relevants.

Presentation of a Case:

- The abdomen is distended, flanks are full and skin is hyperpigmented.
- Umbilicus is everted.
- Superficial veins are visible with normal flow (away from umbilicus).
- Liver is palpable, . . . cm from right costal margin in the midclavicular line, non-tender, firm in consistency, with smooth surface and sharp margin. There is no hepatic bruit.
- Spleen is palpable, . . . cm from the costal margin in left anterior axillary line, towards the right iliac fossa.
- Fluid thrill and shifting dullness are present.

My diagnosis is Hepatosplenomegaly with ascites.

Q: What is the likely cause?

A: CLD with portal hypertension.

Q: What else do you like to see?

A: Stigmata of CLD.

Q: In this middle-aged lady, what may be the cause?

A: May be due to HBV or HCV or primary biliary cirrhosis.

Q: If it is PBC, what else do you like to see?

A: As follows:

- Jaundice.
- Xanthelasma.
- Xanthomatous deposit (in elbow, knee, buttock, hand crease and tendo-calcaneus).
- Pigmentation (may be generalized).
- Scratch mark of itching.

Q: What are the diseases associated with PBC?

A: PBC is an autoimmune disease. It may be associated with other autoimmune diseases such as:

- Sjogren's syndrome.
- Thyroid disease (hypothyroidism or Grave's disease).
- Systemic sclerosis.
- Keratoconjunctivitis sicca (dry eyes and mouth) is seen in 70% of cases.
- Rheumatoid arthritis.
- Renal tubular acidosis.
- Dermatomyositis.
- Addison's disease.
- Membranous glomerulonephritis.
- Fibrosing alveolitis.
- Coeliac disease.
- Interstitial pneumonitis.

N.B. There is high incidence of coeliac disease in PBC, suspected when a patient suffers from malabsorption.

Q: How the patient with PBC usually presents?

A: Common in females, middle-aged, of 40 to 60 years of age. F:M ratio is 9:1. More in smokers.

- May be asymptomatic, isolated hepatomegaly on routine examination. High alkaline phosphatase in LFT.
- Pruritus may be the early feature, may precede jaundice by many months.
- Jaundice (usually with pruritus).
- Abdominal pain or discomfort.
- Features of malabsorption.
- Fever, malaise, weakness, loss of weight.
- Others: hepatic osteodystrophy (characterized by bony pain or fracture due to osteomalacia or osteoporosis from malabsorption).

READ THE FOLLOWING TOPICS IN RELATION TO PBC

Q: What is primary biliary cirrhosis? What are the causes?

A: PBC is a chronic, progressive, cholestatic liver disease characterized by granulomatous destruction of interlobular bile ducts, inflammatory damage with fibrosis spreading from portal tract to liver parenchyma and eventual cirrhosis.

Causes: Actual cause is unknown, probably auto-immune disease occurring in genetically predisposed person (HLA DR-8) via molecular mimicry, initiating auto-immunity. Infection with *Novosphingobium aromaticivorans* or *Chlamydomyxa pneumoniae* may trigger or cause PBC. Urinary tract infections (caused by *E coli* or *Lactobacillus delbrueckii*), smoking and possibly hormone replacement therapy, hair dye are risk factors.

Q: What is secondary biliary cirrhosis?

A: When cirrhosis develops due to prolonged obstruction of the large biliary ducts. Causes are stone, strictures and sclerosing cholangitis.

Q: What is antimitochondrial antibody (AMA)?

A: It is an antibody directed against mitochondrial pyruvate dehydrogenase complex (PDC) of mitochondrial enzymes. 9 types of antigens of which antibodies to M2, M4, M8 and M9 are associated with PBC. M2 is more specific for PBC. Five M2-specific antigens have been further identified, of which E2 component of PDC is the major M2 autoantigen.

AMA is present in 95% cases of PBC, detected by ELISA (>1:160). It may be positive in autoimmune hepatitis (20%). Other causes are Sjögren's syndrome, systemic sclerosis, asymptomatic recurrent bacteriuria in women, pulmonary tuberculosis and leprosy. It is not related to severity and prognosis.

Q: Why itching in PBC?

A: Actual cause is unknown but probably due to upregulation of opioid receptors and increased level of endogenous opioids. So, opioid antagonist (naltrexone) is used to control itching in PBC.



Xanthoma in elbow



Xanthoma in palm



Xanthoma in buttock



Xanthelasma in PBC



Xanthoma in tendo calcaneus

Q: What investigations are done in PBC?

A: As follows:

- LFT (alkaline phosphatase is very high. Aminotransferases may be high, but not more than five times of the upper limit. γ -glutamyl transpeptidase is also high. Serum total protein and albumin is reduced. There is marked rise of 5-nucleotidases activity).
- USG (shows hepatomegaly with cirrhotic change, splenomegaly and ascites).
- CT scan of whole abdomen.
- Antimitochondrial antibody is positive in 95% cases (M2 is 98% specific). Other antibodies such as anti-smooth muscle antibody (35%) and anti-nuclear antibody (25%) may be present.
- Liver biopsy (shows infiltration of lymphocytes and plasma cells in portal tract, destruction of small bile duct with ductal proliferation, piecemeal necrosis and cirrhosis. Granuloma may be present in 40% cases).
- ERCP or MRCP (to rule out extrahepatic biliary obstruction in doubtful cases).
- Others: Serum cholesterol and immunoglobulin (IgM) are very high.

N.B.: Serum cholesterol may be very high but increased mortality secondary to atherosclerosis is uncommon. Statins may be used with monitoring of LFT.

Q: What are the causes of granuloma in liver?

A: As follows:

- PBC.
- Tuberculosis.
- Sarcoidosis.
- Brucellosis.
- Parasitic (strongyloidiasis).
- Schistosomiasis.
- Drug (phenylbutazone).

Q: What is the best indicator for prognosis?

A: Serum bilirubin (if >100 mmol/mL, liver transplantation should be considered).

Q: How to treat PBC?

A: As follows:

- Ursodeoxycholic acid (UDCA) 10 to 15 mg/kg (It improves bile flow, replaces toxic hydrophobic bile acid in bile acid pool, reduces apoptosis of biliary epithelium. It also improves LFT, slows down histological progress).
- For pruritus: cholestyramine, 4 to 16 gm/day orally, usually with orange juice. Main dose (8 gm) is given before and after breakfast (as duodenal bile acid secretion is more). Rifampicin 300 mg/day or naltrexone (opioid antagonist) 25 mg/day up to 300 mg/day may be given. Naloxone is an alternative. In intractable itching, plasmapheresis, liver-support device (molecular absorbent recirculating system) or liver transplantation may be considered. Anti-histamine has no role, may aggravate encephalopathy.
- Vitamins A, D, E, K supplement.
- If osteoporosis: calcium and vitamin D3, bisphosphonate (such as risedronate may be used).
- Liver transplantation should be considered in liver failure. 5-year survival is over 80%, but recurrence of PBC after transplantation occurs in 1/3rd cases at 10 years.
- Colchicine 0.6 mg orally twice daily and methotrexate 15 mg/weekly may be helpful in improving symptoms in some cases.
- Steroid improves biochemical and histological disease, but aggravates osteoporosis and other side effects, should not be used.
- Azathioprine, penicillamine and cyclosporine have no beneficial role.

Q: What are the indications of liver transplantation in PBC?

A: As follows:

- Advanced liver disease (increasing jaundice with serum bilirubin >100 μ mol/L).
- Intractable pruritus.

Q: What is the recurrence after liver transplantation?

A: Recurrence may occur: 15% at 3 years and 30% at 10 years.

Q: How cholestyramine acts?

A: It is a chelating agent, acts by binding pruritogens in intestine and increases excretion in stool. It is ineffective in complete biliary obstruction.

Q: What is the **prognosis** of PBC?

A: As follows:

- If asymptomatic or if the patient presents with pruritus: Survive for more than 20 years.
- Once symptoms like jaundice develop, average survival is around 5 years (may be 7 to 10 years).

Q: What is the risk of **hepatobiliary malignancy** in PBC?

A: It is increased in PBC. Risk factors for malignancy are older age, male sex, prior blood transfusion, signs of cirrhosis and portal hypertension.

HEPATOMEGALY (DISCUSSION ABOUT HAEMOCHROMATOSIS)

Instruction by the examiner:

- Look at the abdomen, what are your findings?
- Examine or palpate the abdomen and see the relevants.

Presentation of a Case:

- The abdomen is distended, flanks are full with everted umbilicus.
- Skin is hyperpigmented.
- Liver is palpable, . . . cm from right costal margin in the midclavicular line, nontender, firm in consistency, with smooth surface and sharp margin. There is no hepatic bruit.
- Spleen is palpable, . . . cm from the costal margin in left anterior axillary line, towards the right iliac fossa.
- Fluid thrill and shifting dullness are present.

My diagnosis is **Hepatosplenomegaly with ascites**.

Q: What is the likely cause?

A: CLD with portal hypertension.

Q: What else do you like to see?

A: Stigmata of CLD. Also, pigmentation in other parts of the body and arthritis.

Q: If pigmentation and arthritis are present, what is the likely diagnosis?

A: Haemochromatosis.

Q: What are your differential diagnoses?

A: Primary biliary cirrhosis.

Q: Can it be due to cirrhosis by HBV or HCV?

A: Unlikely. Because in such case, liver is usually small.

Q: If PBC, what are the findings?

A: PBC is common in middle aged female with generalized itching. Also, there may be xanthelasma, xanthoma etc.

Q: What is the size of liver in cirrhosis? What are the causes of cirrhosis with enlarged liver?

A: In cirrhosis, liver is usually small. However, liver is enlarged if cirrhosis is due to haemochromatosis and primary biliary cirrhosis. Also in alcoholic cirrhosis (early stage).

Q: What are the causes of haemochromatosis?

A: It may be primary and secondary:

1. Primary: Hereditary disorder, inherited as autosomal recessive trait.
2. Secondary: Causes are—
 - Haemolytic anaemia such as: β -Thalassaemia major, chronic haemolytic anaemia due to other cause, pyruvate kinase deficiency.
 - Sideroblastic anaemia.
 - Exogenous iron overload: Repeated blood transfusion (transfusion siderosis), repeated iron injection, prolonged oral iron.
 - Chronic liver diseases: Hepatitis C, porphyria cutanea tarda, alcoholic cirrhosis (in advanced stage).

READ THE FOLLOWING TOPICS IN RELATION TO HAEMOCHROMATOSIS

Q: What is **primary haemochromatosis**?

A: This is a hereditary disorder, inherited as autosomal recessive trait caused by a mutation in the HFE gene on chromosome 6, characterized by excess deposition of iron in various organs, leading to fibrosis and functional organ failure. It is associated with HLA-B₃, B₇ and B₁₄, more in male, less in female. But in postmenopausal case, it is more in female.

N.B.: Normal body iron is 3 to 4 gm. In haemochromatosis, it may be 20 to 60 g. mainly iron is deposited in liver and pancreatic islets, also in endocrine glands (pituitary, adrenal), heart and skin.

Q: Why haemochromatosis is **less in female**?

A: Females are protected by iron loss in menstruation and pregnancy.

Q: What is the **mechanism (pathogenesis)** of primary haemochromatosis?

A: In haemochromatosis, absorption of iron is more and inappropriate to the body needs. Ultimately progressive and excessive accumulation of iron causes elevation of plasma iron, increase saturation of transferrin and high level of ferritin, which is deposited in different organs of the body.

Q: What are the **clinical features** of haemochromatosis?

A: Usually it occurs in male above 40 years. Common features are:

- Liver involvement: Hepatomegaly, CLD (about 30% may develop HCC).
- Skin pigmentation (lead-en-grey skin pigmentation due to melanin deposition), present in 90% cases.
- Diabetes mellitus.
- Cardiac dysfunction (may cause dilated cardiomyopathy, CCF, arrhythmia).
- Arthritis and chondrocalcinosis (also called pseudogout, secondary to calcium pyrophosphate deposition are also common). Most commonly affected joints are MCP and interphalangeal joints.
- Hypogonadism: Impotence, loss of libido due to testicular atrophy (hypogonadism is usually due to deposition of iron in pituitary).

N.B. Patient with CLD, if cardiac disease, arthritis, skin pigmentation and diabetes, haemochromatosis is very likely.

Q: What **type of diabetes** occurs in haemochromatosis?

A: Bronze diabetes due to bronze colouration of the skin.

Q: What are the common **causes of skin pigmentation**?

A: As follows:

- Addison's disease.
- Haemochromatosis.
- Kala-azar.
- Arsenicosis.
- Drugs: Amiodarone, busulphan, bleomycin, phenothiazine, phenytoin, psoralen.
- Systemic sclerosis.
- Alkaptonuria.
- Nelson's syndrome.
- Chronic debilitating illness (such as malignancy, CLD, CKD).

Q: What are the causes of raised ferritin level?

A: As follows:

- Haemochromatosis due to any cause.
- Adult Still's disease.
- Alcoholic liver disease.
- Hepatitis C infection.
- Non-alcoholic steatohepatitis (NASH).
- As an acute phase reactant in inflammatory and neoplastic conditions.

Q: What investigations should be done in haemochromatosis?

A: As follows:

1. CBC.
2. Liver function tests.
3. Iron profile:
 - Serum iron (increased).
 - TIBC (>70% is saturated).
 - Serum ferritin (increased, >600 µg/L).
4. CT scan or MRI of hepatobiliary system (increased density of liver due to iron deposits). MRI has high specificity for iron overload, but less sensitivity.
5. Hepatic iron index (HII): Shows quantification of liver iron, HII >1.9 suggests genetic haemochromatosis.
6. Liver biopsy (shows iron deposition, hepatic fibrosis, cirrhosis). Liver biopsy to measure iron stores is definitive.
7. Others: Blood sugar, ECG, X-ray chest, echocardiogram, X-ray of the involved joint (shows chondrocalcinosis). If cardiac involvement with restrictive or dilated cardiomyopathy, cardiac MRI is most sensitive to detect cardiac iron deposition.

Q: How to screen for haemochromatosis?

A: All first degree family members must be screened to detect early and asymptomatic disease (by *HFE* mutation analysis, transferrin saturation and serum ferritin). In general population, serum iron and transferrin saturation are the best and cheapest tests available.

Q: What is the cause of death of haemochromatosis?

A: Death is usually due to cardiac failure (30%), hepatocellular failure or portal hypertension (25%), HCC (30%).

Q: How do you treat haemochromatosis?

A: As follows:

- Avoid foods rich in iron (such as red meat), alcohol, vitamin C, raw shellfish, also iron therapy.
- Weekly or twice weekly venesection of 500 ml blood (removes 200 to 250 mg of iron) until serum ferritin is normal. It may take 2 years or more. Aim is to reduce ferritin to <50 µg/L. Then, venesection is continued as required to keep the serum ferritin normal (usually 3 to 4 venesections/year is needed). Following venesection, most of the symptoms improve or disappear, except testicular atrophy, diabetes mellitus and chondrocalcinosis. Joint pain may even worsen.
- Proton pump inhibitor may be given. It reduces intestinal iron absorption.

- Chelation therapy with desferrioxamine (40 to 80 mg/kg/day subcutaneously) may be given. It removes 10 to 20 mg of iron/day, mainly used if the patient cannot tolerate venesection, especially those with cardiac disease or severe anaemia. Oral chelators, deferasirox, 20 mg/kg once daily and deferiprone, 25 mg/kg three times daily, may be given.
- Symptomatic treatment of cirrhosis, diabetes mellitus (usually by insulin), CCF and cardiac arrhythmia.
- Alcohol must be avoided.
- Testosterone replacement is often helpful in hypogonadism.

N.B.: In primary haemochromatosis, iron is deposited in hepatocytes, but in secondary iron overload, iron accumulates in Kupffer cells.

Q: What is the **risk of hepatoma** in haemochromatosis?

A: HCC usually occurs as late sequelae in patient with cirrhosis. Does not occur if treated in pre-cirrhotic stage. In presence of cirrhosis, venesection reduces but does not abolish the risk of HCC.

Q: What is the **prognosis**?

A: If diagnosed and treated in pre-cirrhotic stage, life expectancy is normal. Even in cirrhotic patients, prognosis is good compared to other causes of cirrhosis. 3/4th cases survive 5 years after the diagnosis.

ABDOMINAL MASS

(Any mass or masses in abdomen described here are other than liver, spleen and kidney).

Once a mass is visible or palpable in the abdomen, **ensure** whether it is intra-abdominal or extra-abdominal, while the patient is in supine position. For this, ask the patient to keep the arms across the upper chest and raise the head upward up to halfway (rising test). Or, ask the patient to raise both the extended legs from the bed (leg lifting test). Now look at the mass. Intra-abdominal mass will either disappear or decrease in size and extra-abdominal mass will be more prominent.

Once a mass is felt, the following points should be seen very carefully:

- Site.
- Size.
- Surface (regular or irregular).
- Margin.
- Consistency.
- Tenderness.
- Mobility (fixed or mobile).

Then, present the case systematically. As for example (mention according to your findings).

- There is a mass in the epigastrium (or other site), which is 5×6 cm in diameter.
- Surface is smooth (or irregular).
- Margin is irregular (or smooth).
- Soft (or hard) in consistency, non-tender (or tender).
- Freely mobile from side to side, or from overlying skin and underlying structure (or fixed).

Examiner may ask—

- **What are the differential diagnoses? Or, what are the causes of the mass?**
- **How to investigate? Or, mention one single investigation (usually USG of whole abdomen).**

You must mention the possible common differential diagnosis according to the site of the mass and also the age of the patient (cause may be different in young middle aged or elderly).

Another example of mass in the anterior abdominal wall (in or under skin)

Instruction by the examiner:

- Look at the abdomen, what are your findings?
- Examine or palpate the abdomen and see the relevants.

Presentation of a Mass in Anterior Abdominal Wall:

- There is a mass in the right upper abdomen, 4 3 5 cm, surface is smooth, margin is slightly irregular, firm in consistency, non-tender and fixed to the overlying skin.

My differential diagnoses are (mention according to your finding):

- Lipoma.
- Fibroma.
- Neurofibroma.

Other causes of mass in the anterior abdominal wall:

- Sebaceous cyst.
- Dermoid cyst.
- Malignant deposit (secondary).
- Melanoma.
- Epigastric hernia.
- Umbilical or paraumbilical hernia.
- Incisional hernia.
- Rectus sheath divarication.
- Haematoma.
- Parietal abscess (if tender mass).

MASS IN DIFFERENT SITES OF ABDOMEN

MASS IN EPIGASTRIUM

Presentation of a Case:

(Present as above).

Q: What are the **causes** of epigastric mass?

A: As follows (mention according to the findings and also age of the patient):

If the patient is young, causes are:

- Lymphoma of stomach.
- Mass in left lobe of liver (hydatid cyst, if tender mass—may be liver abscess, rarely hepatoma).
- Epigastric hernia.
- Pancreatic pseudocyst.

If the patient is middle-aged or elderly, the causes are:

- Mass in left lobe of liver: Hepatoma, secondaries and hydatid cyst.
- Mass in the stomach: Carcinoma of stomach, lymphoma.
- Mass in pancreas: Carcinoma of head of the pancreas, pancreatic pseudocyst.
- Mass in transverse colon: carcinoma.

Also mention the cause according to the following findings:

1. In liver:
 - Hard mass: may be due to hepatoma, secondaries (may be hydatid cyst).
 - Cystic mass: may be due to hydatid cyst.
 - Tender mass: may be due to liver abscess, rarely hepatoma.
2. In pancreas:
 - Soft and cystic mass: may be due to pancreatic pseudocyst.
 - Hard mass: may be due to carcinoma of head of the pancreas.
3. In stomach:
 - Hard mass: may be due to gastric carcinoma.
 - Soft to firm (even hard) mass: may be due to gastric lymphoma.
4. Hard mass in transverse colon: may be due to carcinoma in transverse colon.
5. Others:
 - Pulsating mass (aneurysm of abdominal aorta).
 - Epigastric hernia (soft, prominent on coughing and reduces on pressure).

Q: What **relevants** do you like to see if there is epigastric mass?

A: As follows:

- Virchow's gland (due to secondaries from stomach).
- Lymph nodes in other parts of the body (lymphoma).
- If hepatic mass is suspected: Look for jaundice, evidence of CLD, primary source (e.g., testicular mass).
- Jaundice, scratch mark, pigmentation etc. (carcinoma head of the pancreas causing obstructive jaundice).

Q: Mention **one investigation** that will help the diagnosis.

A: USG of whole abdomen.

Q: What **investigations** should be done in this case?

A: As follows (mention according to the suspicion of causes):

1. USG (It will give a clue about mass—hepatic, pancreatic, stomach or colon).
2. Other investigations according to the findings in ultrasonography:
 - If gastric mass: Endoscopy and biopsy (to diagnose carcinoma of stomach and lymphoma).
 - If hepatic mass: Investigate accordingly (e.g., hepatoma, secondaries and hydatid cyst).
 - If pancreatic mass: CT scan, MRI or ERCP.
 - If colonic mass: Barium enema, colonoscopy and biopsy.

MASS IN RIGHT ILIAC FOSSA

Presentation of a Case:

- There is a mass in right iliac fossa (then, describe the mass as above).

Q: What are the causes of **mass in right iliac fossa**?

A: Tell the causes according to the age of the patient:

If the patient is young or early-aged:

- Appendicular lump (tender).
- Ileocaecal TB.
- Crohn's disease.
- Lymphoma.
- Amoeboma (less common nowadays, because of wide use of metronidazole).
- Others: actinomycosis, *Yersinia* infection, tubo-ovarian mass in female, pelvic kidney, ectopic kidney, tumour of undescended testes.

If the patient is elderly or middle-aged:

- Appendicular lump (tender).
- Ileocaecal TB.
- Carcinoma of caecum (hard, irregular and non-tender).
- Lymphoma.
- Others may be as above.

N.B. If there is scar mark in lumbar area, diagnosis is transplanted kidney.

Q: How to **diagnose**?

A: History of the patient, physical examination and investigation.

Q: Mention **one investigation** that will help the diagnosis.

A: USG of whole abdomen.

Q: What investigations do you suggest?

A: According to suspicion of causes:

- Hb%, TC, DC and ESR (leucocytosis in appendicular mass, ESR is high in TB).
- USG of whole abdomen.
- If ileocaecal TB: chest X-ray, MT.
- CT or MRI of abdomen.
- FNAC (CT-guided or USG-guided).
- Barium enema (double contrast).
- Barium meal and follow-through with spot film in ileocaecal region (for TB and Crohn's disease).
- Colonoscopy and biopsy.
- If still no diagnosis is possible, then laparoscopy and biopsy.
- Occasionally, laparotomy may be required.

MASS IN LEFT ILIAC FOSSA

Presentation of a Case:

There is a mass in left iliac fossa (then, describe the mass as above).

Q: What are the causes of mass in left iliac fossa?

A: Causes are (mention according to the age of the patient):

If the patient is young (or also any age), the causes are:

- Thick colon (in irritable bowel syndrome).
- Faecal mass (mass indented and moulded by pressure).
- Occasionally, normal colon may be palpable.
- Carcinoma of colon (rare).
- Diverticulitis.
- Tubo-ovarian mass in female.
- Pelvic kidney.



Mass in left iliac fossa

If the patient is elderly, the causes are:

- Faecal mass.
- Carcinoma of colon (descending or sigmoid colon).
- Diverticulitis (tender, mobile mass).
- Thick colon (in irritable bowel syndrome).

N.B. If laparotomy scar is present, the diagnosis is transplanted kidney. Look for AV fistula and anaemia.

Q: What **investigations** do you suggest?

A: As follows:

- USG of whole abdomen.
- Stool for occult blood.
- Barium enema (double contrast).
- Sigmoidoscopy and biopsy (if needed).
- CT or MRI of abdomen.
- FNAC (USG-guided or CT-guided).
- Laparoscopy.
- Occasionally, laparotomy may be needed.

MASS IN RIGHT HYPOCHONDRUM

Presentation of a Case:

There is a mass in right hypochondrium (then, describe the mass as above).

Q: What are the likely **causes of mass in right hypochondrium**?

A: As follows:

- Mass in liver (hepatoma, secondaries, hydatid cyst).
- Gall bladder mass (carcinoma, mucocoele or empyema of gall bladder).
- Carcinoma of colon (usually in hepatic flexure).
- Carcinoma head of pancreas.
- Right supra-renal mass (e.g., adenoma).

Causes of palpable gall bladder without jaundice:

- Mucocoele.
- Empyema.
- Occasionally, carcinoma of gall bladder.

Causes of palpable gall bladder with jaundice:

- Carcinoma of head of pancreas.
- Carcinoma of ampulla of Vater.
- Stone in common bile duct.
- Pressure from outside on bile duct (lymphoma, secondaries).
- Cholangiocarcinoma.
- Sclerosing cholangitis.

Q: What **investigations** do you suggest?

A: As follows:

- USG of hepatobiliary system.
- LFT.
- CT or MRI.
- Barium enema (double contrast), if carcinoma colon is suspected.
- MRCP or ERCP.
- FNAC (USG-guided or CT-guided) may be needed.
- Laparoscopy (if needed).

Q: Could it be **gall stone** with palpable gall bladder?

A: Unlikely (but gall bladder is palpable, if the stone is in common bile duct).

Q: What is **Courvoisier's law**?

A: It is as follows:

- In a jaundiced patient with palpable, non-tender gall bladder, the cause is unlikely to be gall stones, rather it is due to carcinoma of head of the pancreas, cholangiocarcinoma, carcinoma of ampulla of Vater and extrinsic pressure in bile duct.

Reverse of the law is:

- Obstructive jaundice without palpable gallbladder is unlikely to be carcinoma head of pancreas and extrinsic pressure in common bile duct.

Exception of the law is:

- Double impaction: Stones, simultaneously occluding the cystic duct and distal common bile duct. The stone in CBD causes obstructive jaundice and stone in the cystic duct leads to muco-coele or empyema of gall bladder.
- Multiple or large stone impacted in Hartmann's pouch.

Q: Why gall bladder is **not palpable** in gall stone disease?

A: Gall stone is associated with chronic cholecystitis and gall bladder is fibrosed, which is unable to enlarge.

MASS IN LEFT HYPOCHONDRUM

Presentation of a Case:

There is a mass in left hypochondrium (then, describe the mass as above).

Causes of mass in left hypochondrium:

- Splenomegaly.
- Hugely enlarged left kidney and left suprarenal mass.
- Carcinoma of the stomach (involving the greater curvature).
- Carcinoma of splenic flexure of colon.
- Carcinoma or any mass on tail of pancreas.
- Omental mass.

Q: What **investigations** do you suggest?

A: As follows:

- USG of whole abdomen (this will show whether it is spleen or other mass).
- Then other investigation should be done according to suspicion of cause.

MASS IN CENTRAL ABDOMEN

Presentation of a Case:

There is a mass in central abdomen, just above and below the umbilicus (then, describe the mass as above).

Causes of mass in central abdomen (according to the age and sex):

If the patient is young or early-aged, the causes are:

- Lymphoma.
- Tuberculosis (tabes mesentericus or lymphadenitis).
- Hydatid cyst.
- Mesenteric cyst.
- In female, ovarian cyst and pregnancy.
- Distended urinary bladder (urinary retention).

If the patient is elderly or middle-aged, the causes are:

- Intra-abdominal malignancy.
- TB (tabes mesentericus or lymphadenitis).
- Lymphoma.
- Metastatic lymphadenitis.
- Hydatid cyst.
- Mesenteric cyst.
- Retroperitoneal growth (sarcoma).
- Distended urinary bladder (urinary retention).

Q: Suggest **one investigation** that will help in the diagnosis.

A: USG of whole abdomen.

Q: Suggest **one investigation** that will confirm the diagnosis.

A: CT-guided or USG-guided FNAC.

Q: What **investigations** do you suggest?

A: As follows (according to suspicion of cause):

- USG (investigation of choice).
- Hb%, TC, DC and ESR.
- If TB is suspected: MT, chest X-ray PA view.
- CT or MRI.
- FNAC (USG-guided or CT-guided).
- Barium enema (double-contrast) or barium meal and follow-through or small bowel enema (Ryle's tube is introduced through mouth and barium is given).
- Colonoscopy.
- Laparoscopy and biopsy (if needed) or laparotomy (in some cases).
- If palpable lymph node: FNAC or biopsy is required.
- If hydatid cyst suspected: Casoni's test, haemagglutination test.

MASS IN LOWER ABDOMEN (HYPOGASTRIUM)

Presentation of a Case:

There is a mass in lower abdomen (then, describe the mass as above).

Q: What are the **causes of mass in lower abdomen**?

A: As follows (mention according to your findings, considering the age and sex of the patient):

- In female: Pregnancy in young, fibroid uterus, ovarian cyst or other ovarian mass (e.g., carcinoma).
- Distended urinary bladder (due to retention of urine).
- Carcinoma of urinary bladder.
- Other intra-abdominal malignancy, lymphoma, dermoid, hydatid cyst.



Mass in lower abdomen

Q: What **investigations** do you suggest?

A: USG of whole abdomen. Other investigation should be done according to the suspicion of cause.

MASS IN FLANK (RENAL MASS)

Presentation of a Case:

There is a mass in the flank, in the right, left or both (then, describe the mass as above).

Q: Suggest **one investigation** that will help in the diagnosis.

A: USG of whole abdomen.

Q: What other **investigations** do you suggest?

A: Investigation should be done according to the suspicion of cause.

Q: What are the causes of unilateral and bilateral renal mass?

A: As follows:

Causes of unilateral renal mass:

- Renal cell carcinoma (in middle-aged or elderly), Wilm's tumour (in children).
- Unilateral hydronephrosis or pyonephrosis.
- Hypertrophied single kidney (if nephrectomy of other kidney or congenital absence of one kidney).
- Large renal cyst.
- Polycystic kidney with single palpable kidney (due to asymmetrical enlargement).
- Right kidney may be normally palpable.

Causes of bilateral renal mass:

- Polycystic kidney disease.
- Bilateral hydronephrosis.
- Diabetic nephropathy in early stage.
- Amyloidosis.
- Rarely, bilateral renal cell carcinoma.

MASS IN THE EPIGASTRIUM (DISCUSSION ABOUT CARCINOMA OF STOMACH)

Instruction by the examiner:

- Examine the abdomen or palpate the abdomen and see the relevants.

Presentation of a Case:

- There is a mass in epigastric region, 9×7 cm, irregular, non-tender, margin is ill-defined, firm in consistency and not freely movable.

My **differential diagnoses** are:

- Carcinoma of stomach.
- Hepatoma or secondaries in the liver.
- Lymphoma of stomach.
- Carcinoma of head of the pancreas.
- Carcinoma of transverse colon.
- Pancreatic pseudocyst.

Q: What else do you like to see?

A: I want to palpate left supraclavicular gland (Virchow's gland, called Troisier's sign). In carcinoma of stomach, there may be metastasis to left supra-clavicular lymph node.

Q: Suggest one investigation.

A: USG of whole abdomen (this will show the nature of the mass, whether from the stomach, liver, pancreas etc.).

Q: Mention one investigation to confirm carcinoma stomach.

A: Endoscopy and biopsy.

READ THE FOLLOWING TOPICS IN RELATION TO CARCINOMA OF STOMACH

Q: What are the **presentations** of carcinoma of stomach?

A: As follows:

1. Any patient above 40 years of age presenting with **3 A's** (Anaemia, Anorexia, Asthenia).
2. Vomiting (if tumour in the pyloric end).
3. Pain in the epigastrium.
4. Dysphagia (if tumour is in the cardiac end).
5. Haematemesis and melaena.
6. Mass in the epigastrium.
7. Only unexplained features of anaemia.

8. Features of metastasis:
 - Hepatomegaly.
 - Virchow's gland.
 - Hard nodule around umbilicus (Sister Mary Joseph nodule).
 - Ovarian involvement (Krukenberg's tumour).
 - Prerectal pouch: A shelf-like mass (Blumer's shelf).
9. Paraneoplastic syndrome (such as acanthosis nigricans, dermatomyositis, thrombophlebitis migrans).

Q: What are the **sites** of carcinoma stomach?

A: As follows:

- Antrum: 50%.
- Body of stomach (greater curvature): 20 to 30%.
- Cardiac end of stomach: 20%.

In Western countries, proximal tumours are becoming more common.

Q: What is the **benign tumour** of the stomach?

A: Leiomyoma.

Q: What are the **types** of carcinoma stomach?

A: As follows:

1. Macroscopic-4 types:
 - Polypoid.
 - Ulcerative.
 - Fungating or cauliflower.
 - Diffuse infiltrative (linitis plastica, rare).
2. Microscopic-2 types:
 - a. Adenocarcinoma (95%) is of 2 types:
 - Intestinal (type 1): arising from areas of intestinal metaplasia (more common, with better prognosis).
 - Diffuse (type 2): arising from normal gastric mucosa (poorly differentiated, occurs in young age with bad prognosis).
 - b. Others: squamous cell carcinoma, non-Hodgkin's lymphoma and leiomyosarcoma.

Q: What are the **causes** or **predisposing factors** for carcinoma stomach?

A: Causes are unknown. Predisposing factors are:

1. Diet:
 - Preservatives in diet: nitrites and nitrates, convert to *N*-nitroso compounds, which are carcinogenic. Nitrate is converted by nitrite reducing bacteria, which colonize in achlorhydric stomach.
 - Diet rich in salted, smoked or pickled food.
 - Diet lacking fresh fruits, vegetables, vitamins C and A may be the contributing factors (diet with high amount of vegetables, fruits and with low salt protects carcinoma stomach).



Virchow's gland (left)



Carcinoma stomach

2. Smoking.
3. Alcohol.
4. Gastric surgery (partial gastrectomy and gastrojejunostomy. It is due to intestinal metaplasia and chronic gastritis).
5. Infection by *H. pylori* causes chronic atrophic gastritis and intestinal metaplasia, which is precancerous. This organism is responsible in 60 to 70% cases, mostly associated with achlorhydria. Chronic inflammation with generation of reactive oxygen species and depletion of antioxidant ascorbic acid are also important.
6. Others: pernicious anaemia, adenomatous gastric polyp, familial adenomatous polyposis, Ménétrier disease, blood group A and first-degree relatives.
7. Rarely, hereditary diffuse gastric cancer families (*HDC-1* mutations), in which diffuse gastric cancers occur in association with mutations of E-cadherin gene. It is inherited as autosomal dominant trait.

Q: What is early gastric cancer?

A: It is defined as 'when carcinoma is confined to mucosa or submucosa regardless of lymph node involvement'. It is associated with 5 years survival in 90% of cases. Many may survive 5 years even without treatment. It may be cured by endoscopic mucosal resection or endoscopic submucosal dissection.

Q: What is linitis plastica?

A: It is the diffuse submucosal infiltration by scirrhous carcinoma. Stomach becomes like a rigid tube (other causes of linitis plastica are lymphoma, sarcoidosis and secondary syphilis).

Q: What investigations are done?

A: As follows:

- Hb%, TC, DC and ESR.
- Barium meal double contrast (filling defect, irregular ulcer, in infiltrating type and stomach looks like tube).
- Endoscopy and biopsy (investigation of choice).
- Stool for occult blood test.
- USG of whole abdomen (to see any metastasis).
- Chest x-ray P-A view (to see any metastasis).
- Gastric lavage for exfoliative cytology (previously done when endoscopy was not available).
- To monitor recurrence: CEA may be done.

For staging:

- CT scan of the chest and abdomen in some cases (to see any metastasis).
- Endoscopic ultrasound is useful for local staging to demonstrate the depth of penetration of the cancer and extension into local lymph nodes.
- Laparoscopy is useful in patients who are considered for surgery to exclude serosal disease.
- PET and CT/PET can be helpful in further delineation of the cancer.

Q: How to treat a case of carcinoma stomach?**A:** As follows:

1. Surgery is the only curative treatment. 5 year survival is 90% if surgery is done in early gastric cancer, but only 10% if done in advanced cases.
 - Total gastrectomy with lymphadenectomy is the operation of choice.
 - Proximal tumours involving the oesophago-gastric junction also require a distal oesophagectomy.
 - Small, distally sited tumours can be managed by a partial gastrectomy with lymphadenectomy and either a Billroth I or a Roux en Y reconstruction.
2. Perioperative chemotherapy: ECF (epirubicin, cisplatin and fluorouracil) has improved 5 year survival.
3. Chemotherapy—not much helpful. **FAM** (combination of 5-Fluorouracil + adriamycin + mitomycin C) may be tried.
4. Biological agent trastuzumab may benefit some patients whose tumours over-express HER2.
5. Palliative:
 - Radiotherapy: Very little role.
 - Endoscopic laser ablation of tumour tissue, if surgery is not possible.
 - Endoscopic dilatation or insertion of expandable metallic stents may be used for relief of dysphagia or vomiting.

GASTRIC LYMPHOMA

It is the second commonest neoplasm of stomach. Among the GIT lymphoma, 60% occurs in the stomach. 95% is low-grade non-Hodgkin's B-cell type. Gastric lymphoma may be:

- Primary: Arise from mucosa-associated lymphoid tissue (MALT).
- Secondary to lymph node involvement in other parts of the body.

Primary gastric lymphoma may be due to *H. pylori* infection. Lymphoid tissue is not found in the normal stomach but lymphoid aggregates develop in the presence of *H. pylori* infection.

85% are low grade and 40% are high grade, when associated with *H. pylori* infection. Chronic antigenic stimulation results in monoclonal lymphoproliferation that may cause low-grade MALT lymphoma.

Symptoms: Similar to that of gastric cancer. Patients with primary gastric lymphoma have stomach pain, ulcers or other localized symptoms, but systemic complaints such as fatigue or fever are rare.

Diagnosis: By endoscopy and biopsy. At endoscopy, the tumour usually appears as a polypoid or ulcerating mass.

Treatment:

- Primary type: Treatment with anti-helicobacter therapy may regress the tumour. If no response, other therapy for lymphoma should be given (radiotherapy or chemotherapy).
- Secondary type: Usual therapy for lymphoma (chemotherapy, radiotherapy).

Prognosis: Varies according to type. Features predicting a favourable prognosis are stage I or II disease, small resectable tumour or tumour with low grade histology and age below 60 years.

MASS IN THE EPIGASTRIUM (DISCUSSION ABOUT CARCINOMA OF HEAD OF PANCREAS)

Instruction by the examiner:

- Look at the abdomen, what are your findings?
- Examine the abdomen or palpate the abdomen and see the relevants.

Presentation of a Case:

- There is a mass in epigastric region, 7×7 cm, irregular, nontender, margin is ill-defined, firm in consistency and not freely movable (the patient is also extremely emaciated).

My **differential diagnoses** are:

- Carcinoma of stomach.
- Hepatoma or secondaries in the liver.
- Lymphoma of stomach.
- Carcinoma of head of the pancreas.
- Carcinoma of transverse colon.
- Pancreatic pseudocyst.

Q: What **relevant** do you like to see if it is carcinoma of the head of the pancreas?

A: Jaundice, scratch marks of itching. Also the patient is emaciated, may be pigmented also (all features are due to obstructive jaundice).

Q: Suggest **one investigation** in this case.

A: USG of whole abdomen (this will also help to exclude other mass in the epigastrium).

Q: What **other investigations** do you suggest?

A: As follows:

1. LFT (bilirubin, SGPT, alkaline phosphatase, prothrombin time. Alkaline phosphatase is usually very high).
2. Endoscopic ultrasound is most sensitive ($>85\%$).
3. CT scan of abdomen (with contrast, if needed).
4. MRI and PET scan may be helpful in some cases.
5. USG or CT guided FNAC: May be done, but not in potentially operable case. It may spread the malignancy to the peritoneum.
6. Tumour markers: CA 19-9 is highly sensitive (80%).
7. Others:
 - Barium meal X-ray with C-loop (it will show widening of the C-loop).
 - Blood glucose.
 - ERCP (to see obstruction, irregularity or distortion of pancreatic duct. Also, helpful to insert stent in obstructive jaundice.).
 - MRCP may be done.
 - Sometimes laparoscopy and laparoscopic USG (in very small lesion).

READ THE FOLLOWING TOPICS IN RELATION TO CARCINOMA OF HEAD OF PANCREAS

Q: What are the **causes** of carcinoma head of pancreas?

A: Actual causes are unknown. Some factors are responsible:

- Age, above 70 years.
- Male, predominant (twice more than female).
- Chronic pancreatitis.
- Excessive use of alcohol, coffee, aspirin.
- Smoking.
- Environmental factors, such as petroleum product and naphthylamine.
- Genetic in 5 to 10% cases. There may be hereditary pancreatitis, multiple endocrine neoplasia (MEN) and hereditary nonpolyposis colon cancer (HNPCC).

Q: What are the **types** of carcinoma of pancreas and the **sites**?

A: Usually adenocarcinoma (90%), which arises from the epithelium of pancreatic duct. Sites are as follows:

- 60% in head.
- 25% in body.
- 15% in tail.

Q: What are the **other tumours** of pancreas?

A: Some tumours may arise from islets cell (insulinoma, gastrinoma, glucagonoma, somatostatinoma, VIPoma etc.). May occur as a part of MEN I (parathyroid hyperplasia or adenoma, pancreatic tumour, pituitary adenoma).

Q: What are the **presentations** of carcinoma of the pancreas?

A: As follows:

- Painless obstructive jaundice, with palpable gall bladder in case of carcinoma of head of pancreas.
- Carcinoma involving the body and tail: Usually presents with pain in the epigastrium, deep seated, dull aching, radiates to the back, more on lying flat, feels better with bending forward (pain is due to involvement of coeliac plexus).
- Loss of weight, anorexia, nausea.
- Mass in upper abdomen (in 20% cases).
- Diabetes mellitus (up to 50%).
- Features of acute pancreatitis.
- Rare features are: thrombophlebitis migrans (arm vein is more involved than leg vein), venous thrombosis, portal hypertension (due to splenic vein thrombosis) and marantic endocarditis.
- Features of metastasis (hepatomegaly).



Carcinoma head of pancreas

N.B. Courvoisier's law: In a jaundiced patient with palpable gall bladder, the cause is unlikely to be gall stones, rather it is due to carcinoma head of pancreas and extrinsic pressure in bile duct. (Reverse of the law: Obstructive jaundice without palpable gall bladder is unlikely to be due to carcinoma head of pancreas and extrinsic pressure in common bile duct.)

Q: How to treat carcinoma head of pancreas?

A: As follows:

1. In early stage, surgical resection (Whipple's operation is performed. In this operation, pancreas, duodenum, draining lymph node and part of mesentery are removed). 5 year survival is 20% after surgery. Survival is improved with adjuvant chemotherapy.
2. Tumours of the body and tail are resected as part of laparoscopic distal pancreatectomy.
3. Other treatment (usually palliative):
 - For obstructive jaundice: Endoscopic insertion of stent to relieve intractable itching.
 - For pain: analgesic, injection of alcohol in coeliac plexus (USG-guided or endoscopic-USG-guided).
 - Chemotherapy: 5-FU, adriamycin and cisplatin may be tried. Combination of 5-FU plus gemcitabine may help to improve the survival in advanced disease. Chemotherapy with FOLFIRINOX (5-fluorouracil, leucovorin, irinotecan and oxaliplatin) improves median survival to 11 months.
 - Radiotherapy is not much helpful.
 - Duodenal obstruction may be found in 20% case. Endoscopic insertion of stent may be done. Sometimes, surgical bypass may be necessary.

Q: What is the prognosis?

A: Prognosis is **bad**, mean survival is <6 months.

- Usual 5-year survival is 2 to 5%.
- Following Whipple's operation, 5 year survival is 5 to 14%.
- If adjuvant chemotherapy is given with 5-fluorouracil, then 5 year survival becomes 21 to 29%.
- Prognosis is better if tumour size <3 cm, no lymph node involvement, no marginal involvement at surgery, ampullary or islet cell tumours.

MASS IN THE EPIGASTRIUM (DISCUSSION ABOUT PANCREATIC PSEUDOCYST)

Instruction by the examiner:

- Look at the abdomen, what are your findings?
- Examine the abdomen or palpate the abdomen and see the relevant findings.

Presentation of a Case:

- There is a mass in epigastric region, 7.3 × 9 cm, irregular, non-tender, margin is ill defined, cystic in consistency and not freely movable.

My **differential diagnoses** are: Mention as in carcinoma head of pancreas.

Q: What is the **likely diagnosis** and why?

A: Pancreatic pseudocyst, as it is soft and cystic.

Q: What are the **presentations** of pancreatic pseudocyst?

A: As follows:

- History of acute pancreatitis, trauma to abdomen.
- May be asymptomatic, if small cyst.
- Anorexia, nausea, vomiting, abdominal pain, weight loss and mass in the epigastrium.

Q: What is **pancreatic pseudocyst**? Why it is called **pseudocyst**?

A: It is the localized peri-pancreatic collection of pancreatic juice and debris, surrounded by granulation tissue, which usually develops in lesser sac following inflammatory rupture of pancreatic duct. It is called pseudocyst, because there is no lining epithelium of cyst.



Pseudocyst of pancreas

Q: What **investigations** do you suggest?

A: As follows:

- USG of whole abdomen (single definitive investigation).
- CT or MRI.
- Serum amylase (persistently high).
- Others (LFTs, blood sugar, urea, creatinine and serum electrolytes).

Q: What are the **causes** of pancreatic pseudocyst? How to **treat**?

A: As follows:

- Acute pancreatitis, usually 1 to 2 weeks after acute attack.
- Chronic pancreatitis.
- Trauma.

Treatment:

- Small cyst, <6 cm, no specific treatment and spontaneous resolution may occur.
- For large cyst: conservative treatment, spontaneous resolution in 4 to 6 weeks.
- If no response or cyst >6 cm, or rapidly enlarging cyst or features of obstruction of bile duct or duodenum, surgery should be done. Cyst is drained to stomach, duodenum or jejunum, after 6 weeks, once pseudocyst is matured. Drainage can be done endoscopically using endoscopic ultrasound. If fails, surgical drainage may be needed.
- Aspiration under USG may be done.

Q: What are the complications of pancreatic pseudocyst?

A: As follows:

- Rupture of the cyst.
- Secondary infection and abscess formation.
- Compression of surrounding structures, obstruction of bile duct or duodenum or blood vessels causing pseudoaneurysm.

MASS IN THE EPIGASTRIUM (DISCUSSION ABOUT ANEURYSM OF AORTA)

Instruction by the examiner:

- Look at the abdomen. What are your findings?
- Examine the abdomen or palpate the abdomen and see the relevants.

Presentation of a Case:

- There is a mass in the epigastric region, which is pulsatile, 3 3 4 cm in diameter, non-tender, margin is well defined, soft in consistency.

My diagnosis is **Aneurysm of abdominal aorta**.

Q: What are the **causes** of epigastric pulsation?

A: As follows:

- Normally, in lean and thin person (palpable, but non-expansile).
- Right ventricular hypertrophy.
- Pulsatile liver (in tricuspid regurgitation).
- Mass overlying aorta (carcinoma of stomach).

Q: How to **differentiate** from aneurysm?

A: To differentiate from aneurysm, place two fingers parallel at the outermost palpable margin. If aneurysm is present, pulsation is expansile (see the fingers that go apart from each other and measure the distance).

Q: What are the **causes** of aneurysm of aorta?

A: As follows:

- Atherosclerosis (commonest cause, 90%, commonly in abdominal aorta below the origin of renal artery).
- Aortitis due to any cause: syphilis (rare now-a-days), Takayasu's disease, giant cell arteritis, Reiter's syndrome and ankylosing spondylitis.
- Mycotic aneurysm (by *Staphylococcus* and *Streptococcus* in atheromatous plaque).
- Cystic medial necrosis (in Marfan's syndrome, Ehlers–Danlos syndrome).
- Collagen vascular disease.
- Trauma.

Q: What is **aneurysm of signs** and **aneurysm of symptoms**?

A: As follows:

1. Aneurysm of signs:
 - When aneurysm involves the ascending aorta, there are signs of aortic regurgitation and pulsation in right side of sternum.
2. Aneurysm of symptoms:
 - When aneurysm involves aortic arch and descending aorta, there are symptoms due to pressure to surrounding structures (dysphagia, hoarseness, stridor and breathlessness).

Q: What are the presentations of abdominal aneurysm?

A: It is 5 times more in males, above 60 years of age and in 25% male children of an affected individual.

1. May be asymptomatic.
2. Pulsatile mass.
3. Intermittent or continuous abdominal pain that radiates to the back, iliac fossa or groin.
4. Sometimes, there may be acute severe pain due to rapid expansion or rupture and can cause collapse.
5. Gradual erosion of the vertebral bodies may cause non-specific back pain.
6. Features of thromboembolism.
7. Compression to surrounding structures can cause:
 - Vomiting (due to pressure on duodenum).
 - Oedema and deep vein thrombosis (due to pressure on inferior vena cava).
8. Rarely, patients with aneurysms can present with severe haematemesis secondary to an aorto-duodenal fistula.

Q: What are the complications of aneurysm?

A: As follows:

- Rupture (into the retroperitoneum, peritoneal cavity or surrounding structures, most commonly the inferior vena cava, causing aorto-caval fistula).
- Thrombosis.
- Embolism.
- Pressure on nearest structure.

Q: What investigations do you suggest?

A: As follows:

- USG of abdomen (investigation of choice).
- Plain X-ray of abdomen (curvilinear calcification may be present).
- CT scan.
- Aortography.
- Others to find out risk factors (blood sugar, lipid profile, VDRL and TPHA).

Q: How to treat aneurysm?

A: As follows:

1. Medical: Control of hypertension, smoking cessation and lipid-lowering agents. If aneurysm is small, <5.5 cm, regular follow up by ultrasound.
2. Surgical: Surgery should be done if the aneurysm is:
 - ≥ 5.5 cm diameter or,
 - Expanding at a rate of > 1 cm/year or,
 - Symptomatic.
 Surgical techniques are:
 - Open surgical repair: Insertion of a Dacron or Gore-Tex graft.
 - Laparoscopic surgery: with hand-assisted laparoscopic surgery (HALS, requiring a midline minilaparotomy) or total laparoscopic surgery (TLS).
3. Endovascular stent insertion (via the femoral or iliac arteries) is a non-surgical approach.

Prognosis: After repair, patients with an AAA should return to normal activity within a few months.

Q: What is dissecting aneurysm? What are the types?

A: It means when there is a tear in intima of aorta, exposing diseased media to blood and creating a false lumen.

Anatomically, it is of 2 types:

- Type A: When involves ascending aorta, may extend to involve descending aorta.
- Type B: When involves descending aorta, below the left subclavian artery.

According to the timing of diagnosis from the onset of symptoms, it is of 3 types:

- Acute: <2 weeks,
- Subacute: 2 to 8 weeks.
- Chronic: >8 weeks.

Mortality and extension decreases with time.

Q: What are the causes or predisposing factors of dissecting aneurysm?

A: Causes or predisposing factors of dissecting aneurysm are:

- Hypertension, commonest cause (80%).
- Aortic atherosclerosis.
- Cystic medial necrosis in aortic wall (Marfan's syndrome, Ehlers–Danlos syndrome).
- Surgery (aortic valve replacement, coronary artery bypass surgery).
- Pregnancy (in the 3rd trimester).
- Coarctation of aorta.
- Fibromuscular dysplasia.
- Trauma.
- Iatrogenic (e.g., cardiac catheterization, intra-aortic balloon pumping).

Q: What are the presentations of dissecting aneurysm?

A: As follows:

1. Sudden severe chest pain, tearing in nature, between shoulder blades.
2. Features of shock.
3. Features like acute myocardial infarction.
4. On examination—
 - Asymmetric radial pulse.
 - Signs of AR.
 - Features of shock may be present.

Q: What investigations should be done?

A: As follows:

- Chest X-ray (shows widening of upper mediastinum).
- ECG (to exclude MI).
- Echocardiogram (trans-oesophageal echocardiogram is highly specific).
- CT or MRI (also highly specific).

Q: How to treat dissecting aneurysm?

A: As follows:

1. When it involves ascending aorta (type A): immediate surgery is necessary (arch replacement).
2. When it involves descending aorta (type B): conservative treatment should be given. Surgery may be necessary later on.
3. Treatment of primary cause: BP must be controlled. Target is to maintain mean arterial pressure 60 to 75 mmHg. First-line therapy is β -blockers (such as labetalol, metoprolol). Rate-limiting calcium channel blockers (such as verapamil or diltiazem) are used if β -blockers are contraindicated.
4. Endovascular intervention with stents may be indicated in the following cases:
 - Rapidly expanding dissections (>1 cm/year).
 - Critical diameter (>5.5 cm).
 - Refractory pain or malperfusion syndrome.
 - Blunt chest trauma.
 - Penetrating aortic ulcers or intramural haematoma (IMH).

Regular follow up of patients should be done with CT or MRI.

MASS IN RIGHT ILIAC FOSSA (DISCUSSION ABOUT ILEO-CAECAL TUBERCULOSIS)

Instruction by the examiner:

- Examine the abdomen or palpate the abdomen and see the relevants.

Presentation of a Case:

- There is a mass in right iliac fossa, 4 3 6 cm, surface is irregular, non-tender, ill-defined margin, firm in consistency and freely movable from underlying structure and overlying skin.

My differential diagnoses are (tell the causes according to the age of the patient):

If the patient is young or early-aged:

- Appendicular lump (usually tender).
- Ileo-caecal tuberculosis.
- Crohn's disease.
- Lymphoma.
- Tubo-ovarian mass in female.
- Others: Pelvic kidney, tumour in undescended testes.

If the patient is elderly or middle-aged:

- Appendicular lump (usually tender).
- Ileocaecal tuberculosis.
- Carcinoma of caecum (usually hard, irregular and non-tender).
- Lymphoma.

N.B. If there is scar mark in lumbar area, diagnosis is transplanted kidney.

Q: Mention **one investigation**.

A: USG of whole abdomen.

Q: What are the **causes** of ileocaecal TB?

A: It is caused by reactivation of primary disease by *M. tuberculosis*. May be secondary to pulmonary TB (by swallowing of sputum). Sometimes, primary TB due to *M. bovis* (rare now-a-days due to pasteurization of milk).

Q: What is the **pathogenesis**?

A: After involvement of mucosa and submucosa, intense inflammation with necrosis occurs in the bowel wall and lymphatics. Caseation is often found.

Q: What is the **type of lesion** and **type of ulcer** in ileocaecal TB?

A: Lesions are ulcerative, hypertrophic or mixed. Ulcer is transverse (in typhoid and Crohn's disease, ulcer is longitudinal).

Q: What are the presentations of ileocaecal TB?**A:** History of pulmonary TB may be present. The patient usually presents with:

- Abdominal pain is the commonest symptom (usually in right iliac fossa, occasionally generalized).
- Features of intestinal obstruction (acute or subacute).
- Features of peritonitis.
- Abdominal distension due to ascites.
- Diarrhoea.
- Features of malabsorption.
- Mass in right iliac fossa.
- General features of tuberculosis: fever, malaise, anorexia, weakness, loss of weight.
- Complication like fistula formation.

Q: What are the complications of ileocaecal TB?**A:** As follows:

- Intestinal obstruction.
- Stricture formation.
- Fistula (entero-enteric or entero-cutaneous).
- Malabsorption.
- Ascites which may be huge.
- Perforation (rare).

Q: What investigations are done to diagnose ileocaecal TB?**A:** As follows:

- CBC and ESR.
- Chest X-ray (shows TB in 50%).
- Mantoux test (MT).
- USG of abdomen.
- CT scan / MRI.
- Barium follow-through with spot film in ileocaecal region.
- FNAC of the mass or lymph node (USG or CT guided).
- Colonoscopy or ileoscopy may be done.
- Sometimes, laparoscopy to see tubercle in peritoneum and biopsy.
- Diagnostic laparotomy (may be necessary).
- If secondary to PTB: sputum for AFB, geneXpert test may be done.

*N.B.: Detection of tubercle bacilli in biopsy specimens by PCR is the most sensitive investigation.***Q: How to treat ileocaecal TB?****A:** As follows:

1. Standard anti-TB chemotherapy (using four drugs).
2. Occasionally, surgery may be needed. Indications are:
 - Intestinal obstruction.
 - Fistula.
 - Perforation.

Q: What is the **duration** of anti-TB regime in ileocaecal TB?

A: Standard 6 months anti-TB therapy is sufficient as in PTB. Previously, anti-TB therapy was extended up to 12 months. But recently, 6 month short course chemotherapy regimen has been found to be as effective as 12 months regimen. However, many still prefers the duration of treatment up to 12 to 18 months.

Q: What is the **role of corticosteroid** in ileo-caecal TB?

A: Use of steroid is controversial. It may be used, may decrease fibrosis, so prevent intestinal obstruction. But steroid may delay healing and predispose to perforation or further obstruction. So, some authority discourages to use steroid.

MASS IN RIGHT ILIAC FOSSA (DISCUSSION ABOUT CROHN'S DISEASE)

Instruction by the examiner:

- Examine the abdomen or palpate the abdomen and see the relevants.

Presentation of a Mass in Right Iliac Fossa

- Describe as in ileocaecal TB. Mention, if any multiple fistula, scar or colostomy bag.

My differential diagnoses are: As in ileocaecal tuberculosis.

Q: What are the **causes** of multiple fistula or sinuses in abdominal wall?

A: As follows:

- Trauma.
- Crohn's disease.
- Abdominal tuberculosis.
- Faecal fistula.
- Actinomycosis.
- Disseminated malignancy.

READ THE FOLLOWING TOPICS IN RELATION TO CROHN'S DISEASE

Q: What are the **sites** of Crohn's disease?

A: Any part of gastrointestinal tract, from mouth to anus, but terminal ileum is commonly involved (hence, it was previously called regional ileitis). In order of frequency, ileum and right side of colon, colon alone, terminal ileum alone, ileum and jejunum. Lesion is transmural (all layers are involved). The disease can involve a small area of the gut, or multiple areas with relatively normal bowel in between them called 'skip lesion'.

Q: What is **Crohn's disease**? What are the **presentations**?

A: Crohn's disease is a chronic inflammatory disease of unknown aetiology involving any part of gastrointestinal tract, commonly the terminal ileum. It is slightly common in female, M:F = 1:1.2, more in young (mean age is 26 years). Common presentations are as follows:

- Frequent diarrhoea.
- Abdominal pain (colicky).
- Weight loss.
- Failure to thrive in children.
- Systemic features are malaise, lethargy, low-grade fever, anorexia, nausea, vomiting.
- Extraintestinal manifestations (see below).
- Patient may present with recurrent aphthous ulceration of mouth, mass in right iliac fossa (due to inflamed loops of bowel matted together or abscess), anal fissures or perianal abscess.
- Sometimes, it may present with acute abdomen (e.g., acute appendicitis). If laparotomy is done, terminal ileum looks oedematous and red.

Q: What are the causes of Crohn's disease?**A:** Actual causes are unknown. Probable factors are:

- Genetic and familial.
- Diet: High sugar and fat, but low residue diet.
- Smoking.
- Probable association with mycobacteria and measles virus (not proved).
- Abnormal immunological response.

N.B. Remember the following points:

- Appendectomy is protective of ulcerative colitis, but may increase the risk of Crohn's disease or may result in more aggressive disease.
- Oral contraceptive pill increases the risk of Crohn's disease.

Q: What is the relation of smoking in IBD?**A:** Incidence of Crohn's disease is high in smokers. But there is increased risk of ulcerative colitis in non-smokers or ex-smokers.**Extra-intestinal manifestations of Crohn's disease:**

- **Eyes:** Conjunctivitis, episcleritis, uveitis or iritis.
- **Mouth:** Aphthous ulcer and thickened lip.
- **Skin:** Erythema nodosum, pyoderma gangrenosum, fistula or scar in abdominal wall.
- **Bones and joints:** Acute arthropathy or arthralgia, ankylosing spondylitis or sacroiliitis and clubbing.
- **Perianal region:** Perianal fistula, skin tag and abscess.
- **Liver or hepatobiliary:** Fatty liver, pericholangitis, sclerosing cholangitis (common in ulcerative colitis), autoimmune hepatitis, cirrhosis of liver, granuloma, liver abscess or portal pyaemia, gall stone and cholangiocarcinoma.
- **Kidney:** Nephrolithiasis (oxalate stone), hydronephrosis and pyelonephritis.
- **Others:** Amyloidosis and venous thrombosis.

Q: What are the differential diagnoses of Crohn's disease?**A:** As follows:

- Acute appendicitis or appendicular lump.
- Ileocaecal TB.
- Carcinoma of caecum.
- Lymphoma.
- Amoeboma.
- Mesenteric adenitis.
- Infections by *Yersinia*, actinomycosis.

Q: What investigations should be done in Crohn's disease?**A:** As follows:

- CBC (anaemia is normocytic, may be megaloblastic due to vitamin B12 deficiency).
- ESR and CRP (both high).
- Total protein and A:G ratio (low albumin).
- Liver function tests (may be abnormal).
- Blood for C/S (if septicaemia is suspected).
- Stool for R/E and C/S (to exclude infective cause like salmonella, shigella, campylobacter, *E. coli*, *Clostridium difficile*).
- USG of whole abdomen.
- Plain X-ray of abdomen in erect posture in acute attack (to see intestinal obstruction, perforation or toxic megacolon).
- Barium follow-through or small bowel enema (detects ileal disease. There may be narrowing of the affected segment called **string sign**, which is pathognomonic of Crohn's disease).
- Barium enema.
- Colonoscopy (in colonic Crohn's disease) with ileoscopy and biopsy.
- Enteroscopy.
- Capsule endoscopy (in assessing small bowel disease).
- CT colonogram or MRI enterography may be done.

Q: How to assess the activity of Crohn's disease?**A: Signs of activity are:**

1. Clinical:
 - Eye signs: Episcleritis, conjunctivitis and iritis.
 - Mouth: Aphthous ulcer.
 - Skin: Erythema nodosum and pyoderma gangrenosum.
 - Arthralgia of large joints.
 - Fatty liver or liver abscess or portal pyaemia.
 - Mesenteric or portal vein thrombosis.
 - Venous thrombosis (in other veins).
2. Morphology: By radiological or endoscopy.
3. Laboratory:
 - Low albumin (due to protein losing enteropathy).
 - High ESR.
 - High CRP.
 - Scanning with white cell labelled with $^{111}\text{Indium}$ or $^{99\text{m}}\text{Tc}$ to locate active site.

Q: What are the types of arthritis in Crohn's disease?**A:** Peripheral arthropathy is common, which may be of 2 types:

- Type 1 (Pauciarticular): Usually acute, self-limiting, <10-weeks duration, occurs with IBD relapses, usually associated with other extra-intestinal features of IBD. Indicates active disease.
- Type 2 (Polyarticular): Lasts longer (months to years), not related to IBD activity, associated with uveitis.

Other types: Ankylosing spondylitis, arthralgia, inflammatory back pain, which are not related to IBD disease activity.

Q: How to treat Crohn's disease?

A: Induction of remission in active disease and maintenance of remission.

Induction of remission:**1. General measures:**

- Diet: high protein, low fat and milk free. If needed, enteral or parenteral feeding.
- For anaemia: Iron, B₁₂, folic acid and zinc. Erythropoietin may be given.
- Calcium and vitamin D supplements.
- Symptomatic treatment for diarrhoea (loperamide, codeine phosphate or cophenotrope). In longstanding diarrhoea, cholestyramine may be helpful.

2. Drugs:

- Prednisolone: 40 to 60 mg/day. After improvement, dose is reduced, 5 mg/week over 8 weeks, then stopped. Budesonide may be used (9 mg once daily for 6 weeks, with a gradual tapering over 2 weeks. Side effect is less than prednisolone).
- Combination of prednisolone and azathioprine or 6-mercaptopurine (6-MP) may be used.
- For perianal disease: metronidazole (400 mg BD for 14 days) **plus** ciprofloxacin. 6-MP or azathioprine may be used in chronic case. Infliximab or adalimumab are effective in healing fistula and perianal disease.
- In active and moderate to severe total Crohn's colitis or ileo-colitis is treated as in active ulcerative colitis.

N.B.: Alternative to steroid, enteral nutrition with either an elemental (constituent amino acids) or polymeric (liquid protein) diet may induce remission. If given for 28 days, induction of remission is similar to steroid. Relapse is high, particularly in colonic involvement. Both types of diet are equally effective but polymeric one is more palatable when taken by mouth. It is more effective in children and in extensive ileal disease in adults.

Treatment of active and moderate to severe total Crohn's colitis or ileo-colitis:

- a. Oral and per-rectal aminosalicylate (mesalazine, olsalazine, balsalazide) plus per rectal steroid should be given.
- b. Oral prednisolone is indicated for more active disease or when aminosalicylate is ineffective.
- c. In more severe colitis or if no response to oral therapy, patient should be hospitalized and treated as follows:
 - IV fluid and nutritional support.
 - IV methyl prednisolone or hydrocortisone 100 mg 6 hourly.
 - Topical and oral aminosalicylates are also used.
 - If no response to steroid therapy: IV cyclosporine or infliximab may be given. Otherwise urgent surgery should be done.

Maintenance of remission:

- Smoking must be stopped.
- Daily thiopurines (azathioprine or 6-MP) is given. Or,
- Weekly methotrexate may be given.
- In aggressive disease: combination of immunosuppressive and anti-TNF therapy should be given (but cost is high and adverse effects are also more).
- Aminosalicylates may be given, but has minimal efficacy.

In resistant cases (to steroid or immunosuppressive) or failure of above therapy, the following treatment may be given:

- Methotrexate.
- IV cyclosporine.
- Anti-TNF antibody e.g., infliximab (5 mg/kg IV infusion) may be given in 3 occasions (0, 2 and 6 weeks) with 8 weeks maintenance thereafter.
- Also, adalimumab may be used.
- Relapse usually occurs after 12 weeks. So, MTX or azathioprine or 6-MP should be added to maintain remission (etanercept is ineffective).
- Infliximab helps in healing fistula and perianal disease.

N.B.: These agents are contraindicated in presence of any infection including tuberculosis. There is increased risk of opportunistic infection and malignancy. Multiple sclerosis may be unmasked.

Surgical management: Surgery should be avoided if possible. If surgery is needed, minimum resection should be done, as the disease is multicentric and recurrence is almost inevitable. Indications of surgery:

- Failure of medical therapy, intractable disease or fulminant disease.
- Complications such as toxic megacolon, obstruction, perforation, massive haemorrhage, refractory fistula, abscess, which are not responding to medical treatment.
- Extra-intestinal complications like severe arthritis or pyoderma gangrenosum not responding to medical treatment.
- Failure to grow in children despite medical treatment.
- Suspicion of malignancy or severe dysplasia.

Recurrence is common after surgery. If second surgery is needed, azathioprine or 6-MP should be added to prevent recurrence. There is no strong benefit, if it is given after first surgery.

N.B. Prednisolone has no role to prevent recurrence.

Q: What are the **differences** between ulcerative colitis and Crohn disease?

A: As follows:

Features	Crohn's Disease	Ulcerative Colitis
1. Age and sex	Any age, more in female	Any age, equal sex
2. Site	Mouth to anus, commonly ileum and right side of colon	Large gut, commonly rectum
3. Presentation	Abdominal pain, diarrhoea, weight loss are common	Bloody diarrhoea
4. Nature	Transmural (all layers of gut wall are involved)	Mucosa
5. Type	Patchy and discontinuous, skip lesions are present	Continuous or confluent
6. Crypt abscess	Less	Common
7. Fistula, perianal or ischiorectal abscess and skin tag	Common	Uncommon
8. Others	Deep ulcers with fissure. Mucosa in between them looks like cobblestone	Pseudopolyps (due to hypertrophy of mucosa)
9. Colon cancer	Less	Common
10. Microscopy: - Granuloma - Goblet cells - Cells	- In 50 to 60% cases, non-caseating granuloma present. - Slight loss or normal - Chronic inflammatory cells with lymphoid hyperplasia	- Absent - Loss or depleted and distorted - Acute and chronic inflammatory cells in lamina propria and crypts
11. Smoking	Common in smoker	Common in non-smoker and ex-smoker

CARCINOMA OF COLON

Instruction by the examiner:

- Examine the abdomen or palpate the abdomen and see the relevants.

Presentation of a Case:

- There is a mass in left iliac fossa (or mass in right iliac fossa in Ca caecum), then describe as mass in left iliac fossa.

My differential diagnoses are (mention according to the age of the patient): See in the mass in right or left iliac fossa described previously.

If the patient is young, the causes are:

- Thick colon (in irritable bowel syndrome).
- Faecal mass (mass indented and moulded by pressure).
- Diverticulitis.
- Occasionally, normal colon may be palpable.
- Tubo-ovarian mass in female.
- Pelvic kidney.
- Carcinoma of colon (rare).

If the patient is elderly, the causes are:

- Faecal mass.
- Diverticulitis (tender, mobile mass).
- Carcinoma of colon (descending or sigmoid colon).
- Thick colon (in irritable bowel syndrome).

Q: What investigations do you suggest in this case?

A: As follows:

- USG of whole abdomen.
- Stool for occult blood.
- Barium enema (double-contrast).
- Sigmoidoscopy and biopsy.
- FNAC (USG-guided or CT-guided).
- Laparoscopy, in some cases.
- Occasionally, laparotomy may be needed.

Q: What are the sites of colorectal carcinoma?

A: As follows:

- Sigmoid colon (25%).
- Rectum (21%).
- Rectosigmoid junction (20%).
- Caecum (20%).
- ascending colon (10%).
- Transverse colon (15%).
- Descending colon (5%).

Q: What is the **most common site** of carcinoma of colon?

A: Sigmoid colon.

Q: What are the **types** of carcinoma of colon?

A: As follows:

1. Macroscopically:
 - Polypoid and fungating.
 - Annular and constricting.
2. Microscopically: Adenocarcinoma.

Q: What are the **causes** or **predisposing factors** for carcinoma of colon?

A: The causes are unknown. Predisposing factors are as follows:

1. Dietary factors:
 - Excess consumption of red meat, saturated animal fat.
 - Less dietary fibres.
 - Less intake of vegetables and fruits (high vegetables and fruits may be preventive for carcinoma).
 - Excess and prolonged sugar consumption.
2. Non-dietary factors:
 - Increasing age.
 - Genetic factors such as benign adenomatous polyp or familial adenomatous polyposis.
 - Hereditary nonpolyposis colonic cancer.
 - Family history of colon cancer.
 - Longstanding extensive ulcerative colitis or Crohn's colitis, especially if associated with primary sclerosing cholangitis.
 - History of breast cancer.
 - Ureterosigmoidostomy.
 - Acromegaly.
 - Pelvic radiotherapy.
 - Alcohol (weak association)
 - Smoking (relative risk 1.5 to 3.0).
 - Obesity and sedentary lifestyle.
 - Cholecystectomy.
 - Type 2 diabetes (hyperinsulinaemia).

Factors that **decrease risk** of colorectal carcinoma:

- Diet: Increased fibre, fruits, vegetable, garlic, milk.
- Exercise (colon only).
- Drugs: Aspirin or other NSAIDs, calcium, folic acid, omega-3 fatty acids, combined oestrogen and progesterone hormone replacement therapy.

Q: What are the **clinical features** of carcinoma of colon?

A: May be asymptomatic. Other features of carcinoma of colon depend on the site:

1. If on the left side, there may be:
 - Bleeding per rectum.
 - Alteration of bowel habit.
 - Mass in left iliac fossa.

2. If on the right side, there may be:

- Alteration of bowel habit.
- Intestinal obstruction.
- Mass in right iliac fossa.

N.B. Any patient over 40 years of age presenting with new large bowel symptoms should be investigated. Alarming symptoms are change in bowel habit, rectal bleeding, anorexia and weight loss, faecal incontinence, tenesmus and passing mucus per rectum.

Q: What investigations should be done in colorectal carcinoma?

A: As follows:

- USG of whole abdomen (to see the mass, metastases, lymph node involvement).
- Sigmoidoscopy or colonoscopy and biopsy (gold standard).
- CT colonography.
- CT scan of whole abdomen or MRI.
- Endoanal ultrasound or pelvic MRI (used for staging of rectal cancer).
- PET scan: for detecting occult metastases and for evaluation of suspicious lesions found on CT or MRI.
- Barium enema (double contrast): May be helpful to see the mass, but CT colonography is more preferable.
- Others: Complete blood count, stool for occult blood, CEA (to see recurrence), X-ray chest.
- FNAC (USG-guided or CT-guided).
- Sometimes, laparotomy may be needed.

Q: How the colorectal carcinoma spreads?

A: As follows:

- Local infiltration through bowel wall.
- By lymphatics.
- By blood.
- Transcoelomic.

Q: How screening and prevention are done in carcinoma of colon?

A: Screening is done in the following way:

- Any person >50 years of age, stool for occult blood test.
- Colonoscopy (gold standard).
- Flexible sigmoidoscopy is an alternative to colonoscopy.
- CT colonoscopy may be used in screening programme.
- For high-risk patients, screening by molecular genetic analysis (very promising, but not widely available).

Prevention:

- Chemoprevention by using aspirin, calcium, folic acid. Cox-2 inhibitor may have some role in prevention.
- Secondary prevention to detect early and pre-cancer stage. It is done by screening.

N.B. Remember the following:

- *Colorectal carcinoma is common in the Western world, less among Asians.*
- *Second common cause of death.*

Q: How to **treat** colorectal carcinoma?

A: As follows:

1. Curative:

- Surgical resection of the tumour with pericolic lymph nodes.
- Adjuvant postoperative chemotherapy (with 5-fluorouracil and folinic acid).
- 1 week course of preoperative radiotherapy may be given to large fixed rectal cancer to make it resectable. It reduces the risk of local recurrence.
- Post-operative radiotherapy reduces the risk of local recurrence in rectal cancer, if operative resection margins are involved.
- Metastatic disease confined to liver or lung should be considered for resection, as this can be potentially curative if there is truly no disease at other sites.
- In some cases with metastatic disease, monoclonal antibodies like bevacizumab or cetuximab, either alone or with chemotherapeutic agents such as irinotecan, may be used.
- Adjuvant chemotherapy: 5-fluorouracil/folinic acid or capecitabine, in combination with oxaliplatin, can reduce the risk of recurrence in patients with Dukes stage C cancers and some high-risk Dukes B cancers.

2. Palliative:

- Surgical resection of the primary tumour is appropriate for some patients with metastases to treat obstruction, bleeding or pain.
- Palliative chemotherapy with 5-FU/folinic acid, capecitabine, oxaliplatin or irinotecan may improve survival.
- Endoscopic laser therapy or insertion of an expandable metal stent can be used to relieve obstruction.
- Patients with advanced metastatic disease may be treated with monoclonal antibody using bevacizumab or cetuximab, either alone or together with chemotherapy.
- Pelvic radiotherapy is sometimes useful for distressing rectal symptoms such as pain, bleeding or severe tenesmus.

HAEMATOLOGY

5

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'... it clearly appears that the blood is the generative part, the fountain of life, the first to live, the last to die, and the primary seat of the soul'
—William Harvey

INTRODUCTION

Haematological diseases selected in the examination mostly include the diseases of blood and lymph nodes. These are commonly selected in any examination as short or long case. Usual cases are:

- Anaemia
- Purpura, echymosis or bruise.
- Splenomegaly or hepatosplenomegaly.
- Lymphaedenopathy.
- Swelling of joint (haemarthrosis).
- Fundoscopy (to see intra-ocular haemorrhage).

Usually examiner used to ask:

- Perform the general examination of this patient (to see anaemia, jaundice, purpura, koilonychia, lymphadenopathy, gum hypertrophy, bony tenderness in leukaemia, frontal or parital bossing in haemolytic anaemia, plethoric face in polycythaemia, DVT).
- Look at the patient (purpuric spot). What is your finding?
- Palpate the abdomen. What are your findings? (splenomegaly or hepatosplenomegaly or para-aortic lymphadenopathy) What relevant do you like to see?

Usual cases are:

- Lymphoma.
- Hereditary haemolytic anaemia (e.g., β thalassaemia major, Hb E disease).
- Chronic myeloid leukaemia.
- Chronic lymphocytic leukaemia.
- ITP (or multiple purpuric spot, ecchymoses or bruise).
- Myelofibrosis.
- Polycythaemia Rubra Vera.

Remember, common haematological symptoms are:

1. Symptoms of anaemia: tiredness, weakness, dizziness, giddiness, breathlessness, palpitation, fatigue.
2. Bleeding—
 - Skin: petechiae, bruises, purpura, ecchymosis.
 - Gum and mucous membrane bleeding.
 - Menorrhagia.
 - Haematemesis, melaena, epistaxis.
 - Fundal haemorrhage.
 - Bleeding into joints (haemarthrosis) or muscles, bleeding into soft tissues.
 - Retroperitoneal haemorrhage.
 - Intracranial haemorrhage.
 - Post-surgical bleeding.
3. Infection, fever, bone pain.
4. Lymph node enlargement.
5. Leg ulcer (in hereditary spherocytosis, macroglobulinaemia, TTP, polycythaemia).
6. Itching (in polycythaemia rubra vera, Hodgkin's disease).

GENERALIZED LYMPHADENOPATHY (HODGKIN'S LYMPHOMA)

Instruction by the examiner:

- Perform the general examination.
- Examine the neck and relevant.

Presentation of a Case:

- This patient has generalized lymphadenopathy involving cervical, supraclavicular, axillary and inguinal lymph nodes which are of variable size and shape, rubbery in consistency, discrete, non-tender, free from underlying structure and overlying skin.

My differential diagnoses are (mention according to the age of the patient):

If the patient is young or child:

- Lymphoma (usually Hodgkin's disease).
- Acute lymphoblastic leukaemia.
- Viral infection (infectious mononucleosis, cytomegalovirus infection).
- Others: Disseminated TB, SLE.

If the patient is middle aged or elderly:

- Lymphoma.
- Chronic lymphatic leukaemia (may be acute lymphoblastic leukaemia).
- Viral infection (infectious mononucleosis and cytomegalovirus infection).
- Others: Sarcoidosis, brucellosis, toxoplasmosis and HIV.
- Disseminated TB.

Q: What **relevant** do you like to see?

A: As follows:

- Liver and spleen (may be found in lymphoma and leukaemia).
- Anaemia and bony tenderness (found in leukaemia).
- Purpura or bruise or petechiae (found in leukaemia).
- Palatal petechial haemorrhage (found in infectious mononucleosis).
- Cachexia (found in disseminated TB).

READ THE FOLLOWING TOPICS IN RELATION TO LYMPHOMA (HODGKIN'S)

Q: What is **lymphoma**?

A: Group of disorders due to neoplastic proliferation of lymphoid tissue. Majority are of B-cell origin.
2 types:

- Hodgkin's disease (HD).
- Non-Hodgkin's lymphoma (NHL).



Right sided cervical
lymphadenopathy



Bilateral cervical
lymphadenopathy



Left sided cervical
lymphadenopathy

Q: What is Hodgkin's disease?

A: It is a type of lymphoma characterized by painless, progressive enlargement of LNs associated with **Reed–Sternberg giant cell** (hallmark of the disease). It usually occurs in adolescence and young adults (20 to 35 years of age), also after 45 years of age (50 to 70 years, two peaks of incidence). Median age is 31 years. More in males than females (1.5:1). Three times more with past history of infectious mononucleosis.

Q: What are the types of Hodgkin's disease?

A: 2 types:

1. Nodular lymphocyte predominant Hodgkin's lymphoma (HL): 5%, slowly growing, localized and rarely fatal.
2. Classical HL, 4 types:
 - Nodular sclerosis (70%, common in young, female).
 - Mixed cellularity (20%, common in elderly, male).
 - Lymphocyte predominance (5%, common in men).
 - Lymphocyte depleted (rare, probably represents large cell or anaplastic NHL).

Q: What are the features or presentations of Hodgkin's disease?

A: As follows:

- May be asymptomatic.
- Generalized lymphadenopathy starting in cervical glands, then axillary, inguinal. Lymph nodes are painless, discrete and rubbery.
- Dry cough, shortness of breath (due to mediastinal lymphadenopathy).
- Systemic features: fever, loss of weight, malaise, weakness and pruritus (10%).
- After alcohol intake, pain at the site of lymph node involvement.

Q: What is Pel–Ebstein fever?

A: Recurrent bouts of pyrexia followed by apyrexial period. May occur in 10% cases of HD.

Q: What investigations are done in HD?

A: As follows:

Routine: For diagnosis:

1. CBC (may be normocytic normochromic anaemia, lymphopenia, high eosinophil, high ESR. Blood count may be normal).
2. Chest X-ray (shows bilateral hilar lymphadenopathy and widening of mediastinal shadow).
3. Ultrasonography of whole abdomen (to see para-aortic lymphadenopathy, hepatosplenomegaly).
4. CT scan of chest and abdomen, pelvis, neck (necessary for staging).
5. PET scan (positron emission tomography): Used for staging, assessment of response and direction of therapy.
6. FNAC or biopsy (Biopsy is more preferable to see the architecture of lymph node that may not be detected by FNAC, also biopsy is necessary for staging).
7. Bone marrow biopsy (for stage III or IV, or HIV-positive patient or patient with B symptoms).

Before specific therapy:

- Electrolytes and renal function (S. creatinine), liver function tests (SGPT), S. LDH.
- Serum uric acid.
- Virology: HIV, hepatitis B and C.
- Cardiac function.
- Respiratory function.
- Fertility.

N.B.: Remember the following points:

- *Lymphopenia, high LDH and lymph node >10 cm are poor prognostic factors.*
- *High ESR is an indicator of disease activity.*
- *High ALP (due to biliary obstruction) indicates involvement of lymph nodes in porta hepatis.*

Q: What is Reed–Sternberg cell?

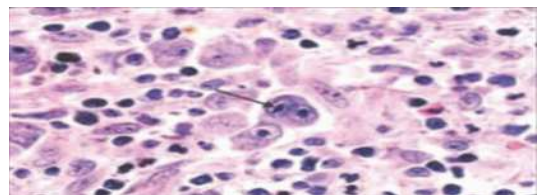
A: It is a malignant cell of B-cell origin, characterized by:

- Large cell with paired mirror image nuclei that resembles ‘Owl’s eye’ appearance.
- Prominent nucleoli.

Reed–Sternberg cell is the hallmark of Hodgkin’s disease. Rarely, found in infectious mononucleosis, recurrent Burkitt lymphoma and chronic lymphocytic leukaemia (CLL).



Reed–Sternberg giant cell



Reed–Sternberg giant cell

Q: What are the stages of HD?**A:** Ann Arbor staging classification:**Stage 1:** Involvement of single LN region (I) or 1 extralymphatic site (IE).**Stage 2:** Involvement of 2 or more lymph node regions on the same side of diaphragm (hilar nodes, when involved on both sides, constitute stage II disease), localized contiguous involvement of only one extranodal organ or site and lymph-node region(s) on the same side of diaphragm (IIE).**Stage 3:** Involvement of lymph-node regions on both sides of the diaphragm (III), which may also be accompanied by involvement of the spleen (IIIS) or by localized involvement of only one extranodal organ site (IIIE) or both (IIISE)

- III (1) With or without involvement of splenic, hilar, coeliac or portal nodes.
- III (2) With involvement of para-aortic, iliac and mesenteric nodes.

Stage 4: Diffuse involvement of one or more extralymphatic tissue (such as bone marrow, liver and lung) with or without LN involvement.**Each stage may be sub-classified into 4:****A:** No systemic features.**B:** With systemic features, such as:

- Weight loss (>10% within previous 6 months).
- Drenching sweats.
- Fever (>38°C).

X: Bulky disease (a widening of the mediastinum by more than 1/3rd or the presence of a nodal mass >10 cm).**E:** Involvement of a single extranodal site that is contiguous or proximal to the known nodal site.*N.B.: Lymphatic structures include LN, spleen, thymus, Waldeyer's ring, appendix and Peyer's patch.***Q: How staging is done and why?****A:** For staging, following tests are done:

- Chest X-ray.
- Bone marrow.
- USG of whole abdomen.
- CT scan (whole abdomen and chest).

Staging is done for selection of therapy (radiotherapy or chemotherapy) and also helpful for prognosis.

Q: How to treat HD?**A:** As follows:

1. Early stage (IA, IIA, no bulk):
 - ABVD (Adriamycin or doxorubicin, Bleomycin, Vinblastine and Dacarbazine), 4 cycles every 2 weeks.
 - Adjunctive radiotherapy (20 to 30 Gy) to the involved lymph nodes after 2 to 4 cycles of ABVD.
 - Treatment response is monitored by CT scan or PET scan.

2. Advanced stage:

- Usually 6 to 8 cycles of ABVD, every 2 weeks is given with involved field irradiation to sites which were initially bulky, or at which there is 'persistent disease' after chemotherapy.
- PET scan should be done. In PET-negative, prognosis is good. PET positive masses indicates fibrosis, so radiation should be avoided.
- Overall, the long-term disease control or cure rates are lower with advanced disease.

3. New regimens, if failure to above therapy (about 25%), the following therapy may be given:

- BEACOPP (bleomycin, etoposide, adriamycin or doxorubicin, cyclophosphamide, oncovin or vincristine, procarbazine, prednisolone).

4. In resistance to chemotherapy:

- Autologous bone marrow transplantation (also called HSCT—Haematogenous stem cell transplantation) may be considered.

N.B.: Other chemotherapeutic regimen that was previously used are:

- *MOPP: Mechlorethamine, oncovin (vincristine), procarbazine and prednisolone.*
- *COPP: Cyclophosphamide, oncovin (vincristine), procarbazine and prednisolone.*

Q: What are the **toxicities** of ABVD chemotherapy?

A: Cardiac toxicity due to doxorubicin and pulmonary fibrosis is due to bleomycin. Infertility and secondary myelodysplasia or AML is low or uncommon with this regime.

Q: What is the **prognosis** of HD?

A: Prognosis depends on the stage:

- Early stage HD: Complete remission in >90% if treated with chemotherapy followed by radiotherapy.
- Advanced stage HD: 50 to 70% can be cured.
- If failure to respond to initial chemotherapy or if relapse within 1 year: have poor prognosis but some may achieve long term survival after autologous bone marrow transplantation.
- If relapses after 1 year initial chemotherapy: long-term survival with further chemotherapy alone may be possible.
- Presence of B symptoms indicate adverse prognosis.

N.B.: Remember the following points:

- Fertility is usually preserved after radiotherapy.
- In young women with mediastinal disease, radiotherapy to the breast may cause breast cancer (hence, needs follow-up).
- Patients who continue to smoke after chest radiotherapy, lung cancer may occur.
- Cardiac disease may occur after supra-diaphragmatic mantle field radiation.
- After chemotherapy, infertility may occur in man (needs counselling and storage of sperm).
- Infertility is less in woman. Premature menopause may occur.
- In 5%, myelodysplasia and acute leukaemia may occur 5 to 10 years after alkylating agent.

Q: What is **disease-free** or **cure** in HD?

A: If no relapse after 5 years of withdrawal of treatment, it is called cure or disease-free.

READ THE FOLLOWING TOPICS IN RELATION TO LYMPHOMA (NON-HODGKIN'S)

Q: What is **non-Hodgkin lymphoma (NHL)**?

A: NHL refers to malignant proliferation of lymphoid cells. Majority are B-cells (70%) and few T-cells (30%).



Axillary lymphadenopathy



Cervical lymphadenopathy

Q: What are the **causes** of NHL?

A: Actual cause is unknown. Probable causes are:

- Chromosomal translocation.
- Viral infection: **Epstein–Barr virus**, human herpes virus 8 (Kaposi Sarcoma Herpes virus), Hepatitis C virus and human T-cell leukaemia virus type 1 (HTLV-1).
- *Helicobacter pylori* is an aetiological factor in gastric MALT lymphoma.
- Immunodeficiency state: congenital and acquired immunodeficiency states such as AIDS, severe combined immunodeficiency disease (SCID), Wiskott–Aldrich syndrome, Coeliac disease.
- Acquired immunodeficiency in organ transplantation is strongly associated with NHL. These are commonly extra-nodal and occur in the first year after transplantation.
- A number of familial cancer syndromes are also associated with NHL.
- In autoimmune disorders, there is high risk of NHL, e.g., Sjogren's syndrome, Hashimoto's thyroiditis.
- Exposure to pesticide, hair dyes, organic solvents etc. may be associated.

Q: What are the clinical features of Non-Hodgkin lymphoma (NHL)?

A: NHL can occur at any age, but peak incidence is 65 to 70 years, slightly more in male. It is multi-centric in origin and spreads rapidly to non-contiguous areas. The disease is usually widespread at the time of diagnosis.

- Common presentations are lymphadenopathy, which are discrete, painless, firm. Waldeyer's ring and epitrochlear lymph nodes are frequently involved.
- Systemic symptoms such as fever, night sweats, weight loss, itching.
- Extranodal presentations are more common than Hodgkin's disease. May involve bone marrow, gastrointestinal tract (stomach), lung, thyroid, skin, testes and CNS. Skin involvement (T-cell lymphoma) presents as Mycosis fungoides and **Sézary** syndrome. Oropharyngeal involvement occurs rarely.
- Compression syndrome may occur, such as paraplegia due to compression of spinal cord by an extradural lymphoma, dysphagia, breathlessness, vomiting, intestinal obstruction, ascites, limb oedema, SVC obstruction.
- Bone marrow involvement is more common in low grade (60%) and less in high grade (10%).
- Hepatosplenomegaly due to involvement of liver and spleen.
- Bone involvement may manifest as pathological fractures with pain.

Q: What are the types (grading)?

A: 2 types or grades (depending on the rate at which the cells are dividing):

Low grade shows the following characteristics:

- Low cell proliferation rate.
- Asymptomatic for many years.
- Slow indolent course.
- Remitting and relapsing course.
- Good response to minimal therapy.
- Incurable, but the patient survives for long time.
- Most nodular lymphoma is of low grade.
- Small cell disease (mature lymphocyte) is associated with low-grade lymphoma.
- No treatment is required, if the disease is not advanced and asymptomatic.
- Median survival up to 12 years.
- Transformation to high grade is associated with poor prognosis, occurs in 3% per annum.
- Bone marrow involvement is more common (50 to 60%).

High grade shows the following characteristics:

- Cell divisions occur quickly.
- Early symptoms are common.
- Fatal, if untreated.
- Responds better to treatment and patient may achieve a long-term remission if treated properly (potentially curable disease).
- 75% respond to initial therapy and 50% are disease free for 5 years.
- Large cell disease (immature lymphoid cells) is of high grade.
- Most diffuse lymphomas are of high grade.
- Bone marrow involvement is less common (10%).

Stages of NHL are much similar to Hodgkin lymphoma (HL), but NHL is more likely to be stage III or IV at presentation.

Q: What investigations are done in NHL?**A:** Similar to HL, in addition to the following:

- Routine bone marrow aspiration, trephine biopsy.
- Immunotyping of surface antigen to distinguish T cell and B cell tumours (done on blood, marrow or nodal material). CD-20 should be done.
- Cytogenetic analysis to detect chromosomal translocations and molecular testing for T cell receptor or immunoglobulin gene rearrangements, if available.
- Immunoglobulin measurement (IgG or IgM paraprotein, to see as markers for treatment response).
- Uric acid.
- HIV testing.

Q: What is Waldeyer's ring?**A:** It is a circle of lymphatic tissue in posterior part of oropharynx and nasopharynx, which includes adenoids and tonsils (pharyngeal, tubal, palatine, lingual tonsil). It is involved in NHL, rarely in HL.**Q: What are the treatment of NHL?****A:** Treatment depends on whether it is high or low grade. Also according to stage.

Low-grade NHL: Not cured by any therapy. So, if the patient is asymptomatic, no therapy. Follow-up should be done.

Indications of treatment are:

- Marked systemic symptoms.
- Bone marrow failure.
- Features of compression: SVC obstruction, spinal cord compression, gut obstruction and ascites.
- Large lymphadenopathy causing discomfort or disfigurement.

Treatment options:

- Radiotherapy, for stage I.
- Chemotherapy: Chlorambucil orally may be used. More aggressive combination therapy may be tried in younger age.
- Monoclonal antibody therapy: Rituximab (anti-CD 20 antibody) is effective in 60% cases. Synergistic effects are seen with standard chemotherapy (R-CVP, R-CHOP or R-Bendamustine).
- Autologous stem cell transplantation can also be given (if failure to chemotherapy).
- Kinase inhibitors: Idelalisib (for relapse follicular lymphoma), ibrutinib (for relapse mantle cell lymphoma).

High-grade NHL:

- Chemotherapy (R-CHOP: rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine and prednisolone), 4 to 6 cycles every 3 weeks.
- R-Bendamustine may also be used.
- Radiotherapy (after 4 cycles of CHOP or R-CHOP): for stage I patients without bulky disease. Radiotherapy is also indicated for residual localized site of bulk disease after chemotherapy, for spinal cord and other compression syndrome.
- Autologous stem cell transplantation for relapse chemosensitive disease.

Q: What is the prognosis?**A:** As follows:

1. Low-grade lymphoma has a slow indolent course. Median survival up to 12 years. Transformation to high grade is associated with poor prognosis, occurs in 3% per annum.
2. In high-grade lymphoma: 75% respond to initial therapy and 50% are disease free for 5 years.
3. Adverse prognostic factors in NHL includes:
 - Age >60 years.
 - Stage III or IV (advanced disease).
 - High serum LDH level.
 - Performance status ECOG 2 or more.
 - More than one extranodal site of involvement.
4. In case of high grade NHL, 5 year survival of patient with adverse prognostic factors (high-risk score) is 25%, while that of patients without adverse prognostic factors (low risk score) is 75%.
5. Relapse is associated with a poor response to further chemotherapy (<10% 5-year survival), but in patients under 65 years, bone marrow transplantation improves survival.

Differences between HL and NHL:		
Features	Hodgkin's Lymphoma	Non-Hodgkin's Lymphoma
1. Age	Bimodal. First peak at 20 to 30 years, second peak at 50 to 70 years	Median age 65 to 70 years.
2. LN involvement	Unifocal, localized to a single axial group (cervical, mediastinal)	Multicentric, more frequent involvement of peripheral LN
3. Mesenteric LN and Waldeyer ring	Rarely involved	Commonly involved
4. Epitrochlear LN	Rarely involved	Commonly involved
5. LN spread	Orderly spread by contiguity	Non-contiguous spread (via blood)
6. Extranodal involvement	Less common, occurs late	More common, occurs early
7. Systemic features or B symptoms	Common	Less common
8. Alcohol-induced discomfort at lymph node site	Present	Absent
9. Pel-Ebstein fever	May occur	Does not occur
10. Pruritus	Common	Less common
11. Reed-Sternberg cells	Present (hallmark)	Absent
12. Bone marrow involvement	Early	Late
13. Prognosis	High cure rate	Low cure rate (low-grade tumours are incurable)

GENERALIZED LYMPHADENOPATHY (CHRONIC LYMPHATIC LEUKAEMIA)

Instruction by the examiner:

- Perform the general examination.
- Examine the neck and relevant.

Presentation of a Case (Elderly or Middle Aged):

- Present as described in generalized lymphadenopathy.

Q: What are your **differential diagnosis**?

A: As follows:

- Lymphoma.
- Acute and chronic lymphatic leukaemia.
- Viral infection (infectious mononucleosis and cytomegalovirus infection).
- Disseminated TB.
- Others: Sarcoidosis, brucellosis, toxoplasmosis, SLE, HIV.

Q: Can it be due to **CML**?

A: Unlikely, usually there is no lymphadenopathy in CML. But in CML, lymphadenopathy may occur in blastic crisis.

Q: How does the patient of **CLL** usually **present**?

A: Common in the elderly, M:F = 2:1, involving B lymphocyte, after 45 years (usually 60 to 70 years).

- May be asymptomatic, diagnosed incidentally during routine blood examination.
- General features, such as malaise, weakness, fatigue, weight loss and night sweating.
- Features of anaemia.
- Recurrent infection.
- Generalized lymphadenopathy (detected on routine examination).
- Hepatosplenomegaly (huge splenomegaly, if autoimmune haemolytic anaemia).

***N.B.:** CLL may present as features of leukaemia but, sometimes also as localized disease (small cell lymphoma).*

Q: What **investigations** do you suggest?

A: As follows:

1. CBC: Hb% (low), leucocytosis (50 to $200 \times 10^9/\text{mm}^3$), differential count shows increased lymphocytes (95%, mostly small lymphocyte), platelet is normal, low or slightly increased.
2. Bone marrow (increased lymphocytes).
3. Others:
 - Reticulocyte (high in autoimmune haemolytic anaemia).
 - Direct Coomb's test (positive in autoimmune haemolytic anaemia).
 - Paraproteins (may be increased).
 - Uric acid (high).
 - Immunophenotyping of B-cell antigen (CD19 and CD23) and T-cell antigen (CD5).

READ THE FOLLOWING TOPICS IN RELATION TO CLL

Q: What is CLL?

A: It is a neoplastic disorder of lymphocyte that usually involves B-lymphocytes and rarely T-lymphocytes (5%). More in male than in female (2:1), occurs usually after 45 years of age.

Q: What are the stages of CLL?

A: 3 stages (**Binet staging**):

Stage A (60%):

- Less than 3 areas of LN involvement.
- No anaemia.
- No thrombocytopenia.

Stage B (30%):

- 3 or more areas of LN involvement.
- No anaemia.
- No thrombocytopenia.

Stage C (10%):

- Anaemia.
- With or without thrombocytopenia.
- Regardless of area of LN involvement.

N.B.: Lymphoid enlargement includes cervical, axillary, inguinal, also liver and spleen.

*Another staging (**Rai staging**):*

- **Stage 0:** Lymphocytosis, no lymphadenopathy, no hepatosplenomegaly, no anaemia or no thrombocytopenia.
- **Stage I:** Lymphocytosis with lymphadenopathy, no hepatosplenomegaly, no anaemia or no thrombocytopenia.
- **Stage II:** Lymphocytosis with hepatomegaly or splenomegaly, with or without lymphadenopathy.
- **Stage III:** Lymphocytosis with anaemia with or without hepatomegaly or splenomegaly or lymphadenopathy.
- **Stage IV:** Lymphocytosis with thrombocytopenia with or without lymphadenopathy, hepatomegaly, splenomegaly or anaemia.

Risk group:

- **Low risk:** Rai stage 0.
- **Intermediate risk:** Rai stages I and II.
- **High risk:** Rai stages III and IV.

Q: Why anaemia in CLL?

A: Anaemia is due to bone marrow infiltration and autoimmune haemolytic anaemia.

Q: How to treat CLL?**A:** Treatment depends on stage:

- **Stage A:** No treatment, unless progression occurs. The patient survives for long time, reassurance and follow-up should be done. Life expectancy is normal in older patient.
- **Stage B:** No treatment, if the patient is asymptomatic.
- **Stage C:** Usually treatment is necessary.

Indications of treatment in CLL:

- Evidence of marrow failure indicated by worsening of anaemia or thrombocytopenia.
- Massive or progressive lymphadenopathy or splenomegaly.
- Doubling of lymphocyte count in 6 months.
- Symptoms (fever, night sweating and weight loss).
- Presence of haemolysis or other immune-mediated cytopenias.
- Recurrent infection.

Mode of treatment:**1. Symptomatic:**

- For anaemia and thrombocytopenia: Prednisolone and blood transfusion. If refractory or recurrent, splenectomy may be done (also indicated for hypersplenism).
- Infection: Antibiotic, immunoglobulin (α -globulin 0.4 g/kg/month).
- Local radiotherapy for LN causing discomfort or local obstruction and symptomatic splenomegaly.

2. Specific:

- Fludarabine alone or with cyclophosphamide or mitoxantrone (with or without steroid) is very helpful. Fludarabine should be avoided in autoimmune haemolytic anaemia as it aggravates anaemia.
- Combination therapy: **FCR** (fludarabine, cyclophosphamide, rituximab) is the first line therapy (Rituximab alone is ineffective).
- Chlorambucil used as palliative therapy in older patient. It reduces WBC count, decreases lymphadenopathy and splenomegaly. Bendamustine is an alternative, used in older and in patient who cannot tolerate FCR.
- Alemtuzumab (anti-CD 52 monoclonal antibody) may be used in patient that progresses after fludarabine.
- Ofatumumab (anti-CD 20 monoclonal antibody) used for treatment in fludarabine or alemtuzumab refractory case.
- Obinutuzumab (anti-CD 20 monoclonal antibody). In combination with chlorambucil, it is superior to either chlorambucil alone or chlorambucil with rituximab.
- Allogenic stem cell transplantation may be given if failure to standard therapies.

Q: What is Richter's syndrome?

A: When CLL is transformed to aggressive high grade lymphoma, it is called Richter's syndrome. Occurs in 5 to 10% cases. Its prognosis is poor with median survival less than 1 year.

Q: What is the prognosis of CLL?**A:** Depends on stage:

- Median survival is about 10 years.
- Stage A may be of normal life expectancy. In stage C, median survival is 2 to 3 years.
- About 50% die from infection, 30% unrelated to CLL. Rarely, acute blastic crisis occur.

SPLENOMEGALY (CHRONIC MYELOID LEUKAEMIA)

Instruction by the examiner:

- Examine the abdomen, or palpate the abdomen. What are your findings?

Presentation of a Case: (Patient is usually Middle Aged or above 40 Years).

- Spleen is hugely enlarged, . . . cm from costal margin in anterior axillary line towards right iliac fossa.

Q: What are the **causes of splenomegaly** in this middle-aged patient?

A: As follows:

- Malaria.
- Kala-azar.
- Chronic myeloid leukaemia (CML).
- Lymphoma.
- CLD with portal hypertension.
- Myelofibrosis.
- Tropical splenomegaly syndrome.

Q: What **relevant** do you want to see in this case?

A: As follows:

- Pigmentation (in kala-azar).
- Lymph nodes (may be found in lymphoma).
- Bony tenderness (in leukaemia).
- Signs or stigmata of CLD (see page 393).
- I would like to take the history of fever (in malaria, kala-azar).

Q: Mention one single **investigation** which will be helpful for your diagnosis.

A: CBC with PBF with malarial parasite. By this, I can diagnose:

- CML.
- Myelofibrosis (it shows pancytopenia, leucoerythroblastic blood picture, tear or pear-drop poikilocyte).
- Kala-azar (CBC shows leucopenia, lymphocytosis and monocytosis. If blood count is repeated after some days, it shows progressive leucopenia. Rarely LD body may be found in buffy coat).
- Malaria.
- Sigs of hypersplenism (shows pancytopenia).

READ THE FOLLOWING TOPICS IN RELATION TO CML

Q: What is the **CML**?

A: CML is a myeloproliferative stem cell disorder resulting in excess proliferation of myeloid cell series with presence of Philadelphia chromosome. It is common in 40 to 60 years, peak is 55 years.

Q: What are the myeloproliferative disorder?**A:** 4 diseases:

- Chronic myelocytic leukaemia.
- Myelofibrosis.
- Polycythaemia rubra vera.
- Essential thrombocythaemia.

These disorders are grouped together in which one disease may transform to another. All myeloproliferative disorders may progress to acute myeloid leukaemia.

Q: How does the patient usually present in CML?**A:** As follows:

- May be asymptomatic (25%).
- Splenomegaly (90%, may be huge in 10%). Patient may complain of mass or discomfort, or heaviness or pain in left hypochondrium.
- Unexplained anaemia.
- General features such as weakness, malaise, loss of weight, night sweating.
- Repeated infection.
- Bleeding (due to thrombocytopenia).
- Hepatomegaly (in 50% cases).

Q: What investigations do you suggest in CML?**A:** As follows:

1. FBC:
 - Leucocytosis (may be very high).
 - Differential count shows increase in myelocyte, promyelocyte, metamyelocyte. Increase in neutrophil, basophil and eosinophil. Few myeloblasts may be present.
 - Platelets are increased.
 - Nucleated red cells are common.
2. Bone marrow study (hypercellular marrow with increased myeloid precursors). Cytogenetic analysis for Philadelphia chromosome, also RNA analysis to see the presence of BCR–ABL gene product.
3. Other tests:
 - Philadelphia chromosome (positive in 95% cases).
 - LAP score (decreases).
 - Serum uric acid (high).
 - Serum vitamin B₁₂ (high).
 - Serum LDH (high).

Q: What are the clinical phases or natural history of CML?**A:** 3 phases:

- Chronic phase: In this phase, disease response to treatment and is easily controlled.
- Accelerated phase: In this phase, disease control is difficult.
- Blastic crisis: In this phase, the disease transforms into acute leukaemia, either myeloid (70%) or lymphoblastic (30%), which is relatively refractory to treatment.

Q: What are the causes of death in CML?**A:** As follows:

- Blastic crisis.
- Secondary infection.
- Myelofibrosis.

Q: How to treat CML?**A:** Treatment depends on the phase whether chronic, accelerated or blastic crisis.**1. Treatment of chronic phase:**

- Imatinib is the drug of choice, 400 mg daily. In some cases, 600 to 800 mg may be given to overcome resistance. It can be continued indefinitely, but should be stopped in pregnancy or planning for pregnancy. It shows 76% (95% in some cases) response with disappearance of Philadelphia chromosome after 18 months (it is a tyrosine kinase inhibitor, acts by blocking the enzymatic action of BCR–ABL fusion protein. It reduces uncontrolled proliferation of WBC. Side-effects are nausea, headache, rash and cytopenia).
- If failure to respond to imatinib: second generation tyrosine kinase inhibitor such as dasatinib or nilotinib or allogenic bone marrow transplantation should be considered. Bosutinib and ponatinib may also be used in resistant case.
- Alternately, hydroxyurea or α -interferon that were previously used for initial control are still useful. However, hydroxyurea does not diminish Philadelphia chromosome or affect blastic crisis. α -Interferon is given alone or with Ara-C. It controls CML in chronic phase in about 70% case and causes disappearance of Philadelphia chromosome in 20% cases. It was a first line drug before imatinib. However, α -Interferon still may be used for women who are planning for pregnancy.
- Allogenic bone marrow transplantation (usually below the age of 40 years and in early chronic phase), 70% curative. Busulphan was used previously. Not used nowadays.

2. Treatment of accelerated phase and blastic crisis:

- Treatment is difficult, imatinib is indicated if the patient has not received it. Dasatinib or nilotinib may also be used.
- Hydroxyurea (hydroxycarbamide) can be effective. It is helpful in palliative use.
- Low dose cytarabine can be given.
- In young patient, stem cell transplantation may be considered.
- Also, it is treated like acute leukaemia.

Q: What are the indications of bone marrow transplantation?**A:** Bone marrow transplantation is indicated if:

- The disease is not well controlled.
- The disease progress after initial control.
- For those who have accelerated phase disease.

Q: What are the therapies that may cure CML?**A:** Bone marrow transplantation (BMT), imatinib and α -interferon.

Q: What is the prognosis of CML?**A:** As follows:

- With imatinib therapy, complete haematological remission in up to 95% cases and 70 to 80% of these have no detectable BCR–ABL transcript.
- Following stem cell transplantation: 70% cure in chronic phase in young patients.
- Without treatment: median survival is 3 to 4 years. Some may survive up to 10 years.
- If blastic crisis: prognosis is poor. Median survival is 6 months.
- CML may transform to myelofibrosis.

Q: What is blastic crisis? How can you suspect blastic crisis clinically?

A: It means the disease is transformed to acute leukaemia. It may be myeloid (70%) or lymphatic type (30%). Occurs in 10% per year, relatively refractory to treatment and is the cause of death in majority of cases. Prognosis is poor in myeloid type.

Blastic crisis in CML can be suspected, if:

- Rapid deterioration of the patient.
- Increasing splenomegaly.
- Blood picture shows increase in number of blast cells and increasing basophil.

Q: What is Philadelphia chromosome?

A: This is a defective and short chromosome 22, resulting from a reciprocal translocation of genetic material between chromosome 22 and chromosome 9 and contains a fusion gene called **BCR ABL-1**. The break on chromosome 22 occurs in the breakpoint cluster region (BCR) and joins with the fragment from chromosome 9 that carries *abl* oncogene. It is positive in 95% case of CML. It may also be found in ALL and AML.

PURPURA

Instruction by the examiner:

- Look at the legs (or hands or abdomen). What is your diagnosis? What else do you want to see?

Look at the following points:

1. Whether they blanch on pressure or not (purpura does not blanch).
2. Whether they are palpable and painful or not (palpable painful purpura is of vascular origin and non-palpable purpura indicates thrombocytopenia).
3. Colour change (progressive colour change in purpura from red to dark pigmented).
4. Distribution of purpura:
 - Buttock, ankle (Henoch–Schönlein purpura).
 - Extensor surface of forearm, dorsum of hand, leg (senile purpura and drugs).
 - Generalized purpura (usually ITP, other purpura).

Presentation of a Case:

- There are multiple purpura involving both the legs below the knee, some are red and some are brown or dark and do not blanch on pressure (mention whether palpable or non-palpable).

My diagnosis is **Multiple purpura**.

Q: What do you think are the **causes** in this case?

A: Mention the causes according to age and sex.

In the **elderly**, the causes are:

- Senile purpura (usually on extensor surface of forearm and leg).
- Drug induced purpura (distribution is like senile purpura) such as steroid, NSAID and anticoagulant.
- Leukaemia.
- Aplastic anaemia.
- Scurvy.
- Paraproteinaemia.

In **young** or **child**, the causes are:

- Idiopathic thrombocytopenic purpura (ITP).
- Henoch–Schönlein purpura (involving buttock and legs).
- Drug induced.
- Acute leukaemia.
- Infections: Viral (dengue) or meningococcal septicaemia.



Purpura



Purpura

Q: What **else** do you want to see in this child? What **history** do you like to take?

A: Purpura in buttock. History of arthritis, abdominal pain, bloody diarrhoea, haematuria (which are due to Henoch–Schönlein purpura).

N.B. In any age, mention the causes as follows (if present):

- *If Cushingoid facies—it is due to steroid.*
- *If patient looks toxic—it is due to septicaemia.*
- *If rheumatoid arthritis, SLE—it is due to steroid or NSAID (or by the disease itself).*

Q: What **else** do you like to examine to find out the cause?

A: As follows:

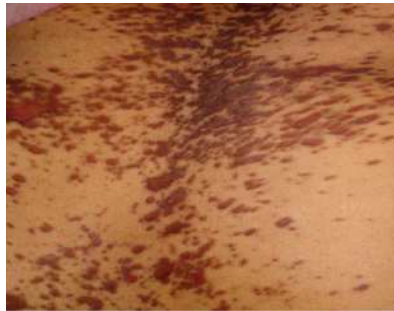
- History of fever—may be dengue haemorrhagic fever or other viral infection, meningococcal septicaemia (the patient looks toxic).
- History of fever, arthritis, bloody diarrhoea, abdominal pain, haematuria (Henoch–Schönlein purpura),
- History of drugs (steroid, NSAID).
- Blood dyscrasia (in Haemophilia, Christmas disease).
- Anaemia (found in leukaemia and aplasia).
- Bleeding gum, corkscrew hair and perifollicular haemorrhage (found in scurvy).
- Any evidence of collagen disease (SLE, RA).
- Evidence of other disease: uraemia, CLD, DIC, metabolic disorder.
- Also examine LNs, liver, spleen and bony tenderness (leukaemia).

Q: What are the differential diagnoses of purpura?**A:** As follows:

- Drug rash.
- Spider angioma or telangiectasia (blanches on pressure, but purpura does not).
- Erythema nodosum (painful and nodular).
- Mosquito bite (usually blanches on pressure, but sometimes may not blanch, if there is extravasation of blood).
- Campbell de Morgan spots (common in elderly): These are small, nodular, reddish lesions that do not blanch on pressure, occur on trunk and upper abdomen, resolve spontaneously. These are benign angioma, common in middle-aged and the elderly. Malignant change occurs rarely (suggested by itching, rapid increase in size and increased pigmentation).



Campbell de Morgan spot



Drug rash



Erythema nodosum

Q: What investigations should be done in purpura?**A:** As follows:

1. CBC, ESR, platelet and PBF.
2. Bone marrow study: If pancytopenia or thrombocytopenia (dry tap in aplastic anaemia, increased megakaryocyte in ITP).
3. Other investigations (according to suspicion of causes):
 - Coagulation screen (BT, CT, PT, APTT).
 - Haemophilia (factor VIII) and Christmas disease (factor IX).
 - APTT, FDP, d-Dimer (if DIC is suspected).
 - Blood culture (septicaemia).
 - ANA, anti-ds DNA (for SLE).
 - Antiphospholipid antibody.
 - Liver function tests (in CLD).
 - Renal function tests (in CKD).

Q: What is Hess test?

A: It is a bedside test, also called tourniquet test. In this test, a sphygmomanometer cuff is inflated over the upper arm between systolic and diastolic blood pressure, kept for 5 minutes and then deflated. Again after 5 minutes, look for petechiae in cubital fossa and near the wrist joint. Normally, there may be <5 petechiae. If >10 petechiae in 2.5 cm² area are observed, it indicates thrombocytopenia. If platelet is <60,000, it is usually positive.

Causes of positive Hess test: It is usually positive in thrombocytopenia or platelet functional abnormality or increase in capillary fragility (This test is frequently done to diagnose dengue haemorrhagic fever in which, if number of petechiae is >20 , it is definitely positive).

READ THE FOLLOWING TOPICS IN RELATION TO PURPURA

Q: What is purpura? What are the causes?

A: It is the spontaneous bleeding or extravasation of blood from the capillary into the skin and mucous membrane that does not blanch on pressure and there is progressive colour change. 2 **types** of purpura:

- Small and discrete of pinhead size called petechiae.
- Large and ill-defined called ecchymosis.

Causes of purpura:

- Thrombocytopenic.
- Vascular.
- Coagulation defect.

Thrombocytopenic purpura:

1. Primary or Idiopathic thrombocytopenic purpura (ITP).
2. Secondary:
 - Aplastic anaemia (due to any cause).
 - Leukaemia.
 - Secondary deposit in bone marrow.
 - SLE.
 - Others: DIC, CLD, TTP (thrombotic thrombocytopenic purpura), massive blood transfusion.

Vascular purpura:

1. Congenital (hereditary haemorrhagic telangiectasia, Ehlers–Danlos syndrome).
2. Acquired
 - Senility (elderly patient).
 - Henoch–Schönlein purpura (in children, and rarely in the adult or elderly).
 - Drug-induced (NSAIDs, thiazide, steroid, sulphonamide, penicillin and thiouracil).
 - Infections: SBE, typhoid, meningococcal infection, septicaemia and viral infections (infectious mononucleosis, measles, chicken pox, dengue haemorrhagic fever).
 - Scurvy.
 - Metabolic disorder (CKD, CLD).
 - Endocrine disorder (Cushing's syndrome).
 - Collagen disease (RA and SLE).
 - Paraproteinaemia (purpura is due to vasculitis or thrombocytopenia or platelet functional abnormality).
 - Amyloidosis (commonly periorbital).

Coagulation abnormality:

- Haemophilia.
- Christmas disease.
- Anticoagulant therapy (heparin, warfarin).

Q: What are the **causes** of platelet functional abnormality?

A: Platelet functional abnormality (thrombasthenia) occurs in:

- CKD.
- CLD.
- Paraproteinaemia.
- Myeloproliferative diseases.
- Drugs: NSAIDs (aspirin, indomethacin and ibuprofen).

Q: How to **differentiate** in bleeding or purpura, whether due to bleeding abnormality or coagulation abnormality?

A: As follows:

Coagulation Abnormality	Bleeding Abnormality
1. Family history usually present	1. Family history may or may not be present
2. There is history of prolonged bleeding	2. No history of prolonged bleeding
3. Usually there is bleeding into the joint or muscle, purpura is less common or rare	3. Bleeding into the skin and mucous membrane, purpura is more common
4. Clotting time is prolonged, but bleeding time and platelet count are normal	4. Clotting time is normal, but bleeding time is prolonged and platelet count is low
5. Particular coagulation factor is low or absent, e.g., in haemophilia, factor VIII is absent or low	5. Coagulation factor is normal, it is due to either low or defect in platelet function or vascular defect

PURPURA (DISCUSSION ABOUT IDIOPATHIC THROMBOCYTOPENIC PURPURA)

Instruction by the examiner:

- Look at the patient. What is your finding?

Presentation of a Case: (Present as in Purpura)

Q: What is **idiopathic thrombocytopenic purpura**?

A: It is a type of thrombocytopenic purpura due to autoantibody against platelet membrane glycoprotein IIb and IIIa (IgG type), which is responsible for premature removal of platelet by monocyte–macrophage system.

Q: What are the **presentations** of ITP?

A: Varies in child or adult:

- **In child:** Usually acute presentation, previous history of viral infection followed by bleeding or purpura, easy bruising etc. Chronic ITP is rare in children. Although bleeding may be severe, life-threatening haemorrhage is rare (1%).
- **In adult:** Common in female, usually insidious onset without preceding viral infection. Presents with purpura, easy bruising, epistaxis or menorrhagia. Features of SLE may be present at presentation or may develop after long time. It may be associated with other autoimmune diseases (thyroid disorder, autoimmune haemolytic anaemia), chronic lymphocytic leukaemia, solid tumour, HIV infection. Platelet autoantibodies are detected in about 60 to 70% patients.

On physical examination: Apart from purpura, no other physical findings. Splenomegaly is very rare.

N.B.: Remember the following points:

- Spontaneous bleeding occurs when the platelet is $<20,000/\text{cmm}$.
- If platelet count is $>50,000/\text{cmm}$, there may not be any features, diagnosed on routine test.



Purpura in ITP (legs)



Purpura in ITP (forearm and hands)

Q: What are the **diseases to be excluded** if ITP is suspected?

A: As follows:

1. SLE. In 10% cases, thrombocytopenia may be the initial manifestation of SLE for many years.
2. Primary antiphospholipid syndrome may present with thrombocytopenia.
3. Other primary haemorrhagic disorders should be excluded.
4. For this purpose, following investigations should be done:
 - ANA, anti-ds-DNA, antiphospholipid antibody and anticardiolipin antibody.
 - Bone marrow study.

Q: How to **investigate ITP**?

A: As follows:

- CBC with platelet count (thrombocytopenia).
- Bone marrow study (increased immature megakaryocytes).
- Bleeding time (prolonged).
- Clotting time (normal).
- Antiplatelet antibody (present).
- ANA (to exclude SLE).
- Antiphospholipid antibody (positive in 30% cases).

N.B.: Remember these points:

- *In 10% case, ITP may be associated with autoimmune haemolytic anaemia called **Evan's syndrome**.*
- *Patient >65 years old, should have bone marrow examination to look for accompanying B-cell malignancy.*
- *In ITP, low platelet in blood, increased megakaryocyte in bone marrow, prolonged bleeding time and normal clotting time are common.*
- *HIV testing should be considered, if there is strong suspicion.*

Q: What are the **differences** between ITP in children and adults (or acute and chronic ITP)?

A: As follows:

Features	Child (Acute)	Adult (Chronic)
1. Age	Usually 2 to 6 years	20 to 30 years
2. Sex	Any	More in female
3. Onset	Acute	Chronic
4. Previous infection	Common	Unusual
5. Platelet count	<20,000/mm ³	>20,000/mm ³
6. Features	Acute	Chronic
7. Spontaneous remission	Common	Less, <20%
8. Duration	2 to 4 weeks	Chronic, months to years

Q: How to treat ITP?**A:** As follows:

In child: Usually self-limiting, does not require treatment in most cases. Treatment is given for serious bleeding or urgent surgery:

- Prednisolone (2 mg/kg), if moderate to severe thrombocytopenia ($<10,000$) and bruising, epistaxis or other bleeding.
- IV immunoglobulin (IgG) may be given, effective in 80%, raises count more rapidly than steroid.
- In some case, platelet transfusion, if persistent bleeding (epistaxis, GIT, retinal haemorrhage, intracranial).

In adult: Persistent thrombocytopenia is common. Most patients with platelet count $>30,000/\text{mm}^3$ do not require treatment and with even lower counts may not require treatment, unless spontaneous bruising or bleeding or surgery.

1. First line therapy:

- If spontaneous bleeding: prednisolone 1 mg/kg, for 4 to 6 weeks, then taper. 66% will respond, but relapse is common when steroid dose is reduced or stopped. Then, steroid should be started again.
- IV immunoglobulin may be given, if severe haemostatic failure or slow response to steroid alone or surgery is required. Dose 1 g/kg for 3 to 5 days. Its effect is temporary, persists for 3 to 4 weeks and is expensive. Steroid may be added with immunoglobulin.

2. Second line therapy:

- Splenectomy: If frequent relapse (>2 relapses) or primary refractory disease or require high dose of steroid to maintain safe platelet level, splenectomy should be done. Complete remission in 70% cases and improvement in 20 to 25% cases. 5 to 10% require further medical therapy.

3. After splenectomy, if severe thrombocytopenia with or without significant bleeding persists—

- Thrombopoietin analogue romiplostim and thrombopoietin receptor agonists eltrombopag may be given.
- Rituximab (anti-CD20). About 60% patients respond, only 15 to 20% have long-lasting responses.
- Ciclosporin and tacrolimus may be considered.

4. Platelet transfusion is not usually used. May be needed if persistent or potentially life-threatening bleeding or where emergency splenectomy is done.

N.B.: Remember the following points:

- In non-responder after splenectomy, think of presence of accessory spleen (confirm by radionuclide scan).
- After splenectomy, more chance of infection by pneumococcus, meningococcus and Haemophilus influenzae. Vaccination against these are essential.

PURPURA (DISCUSSION ABOUT HENOC–SCHÖNLEIN PURPURA)

Instruction by the examiner:

- Look at the patient. What is your finding? What may be the cause?

Presentation of a Case: (Present as in Purpura)

My differential diagnoses are (if the patient is child):

- ITP.
- Henoch–Schönlein purpura (HSP).

Q: What **else** do you want to see if HSP?

A: Buttock. In Henoch–Schönlein purpura, commonly buttock is involved.

Q: What **history** do you like to take in Henoch–Schönlein purpura?

A: Arthritis, abdominal pain, bloody diarrhoea and urinary complaint (haematuria).

Q: What are the **differential diagnoses** in this case?

A: Mention considering the age:

- Drug rash.
- ITP.
- SLE.
- Septicaemia.
- Thrombotic thrombocytopenic purpura (TTP).

READ THE FOLLOWING TOPICS IN RELATION TO HSP

Q: What is **Henoch–Schönlein purpura** (anaphylactoid purpura)?

A: It is a small vessel vasculitis characterized by purpura or petechial rash, polyarthritis (in big joints), abdominal pain and glomerulonephritis. It is due to circulating IgA containing immune complex. Occurs 1 to 3 weeks after upper respiratory tract infection (usually viral). Other factors are food, drugs or vaccination.

Q: What are the **clinical features** of HSP?

A: HSP is more common in boys of 5 to 15 years of age, but may occur at any age. Common features are (4 systems are involved such as skin, joint, abdomen, kidney):

- Skin lesion: Purpura is common in legs and buttock, face and trunk are spared. May resolves in 2 to 4 weeks and fresh crops may appear. Angio-oedema occurs in 50% cases.
- Polyarthritis: In 70%, commonly involves knee and ankle, may be fleeting type.
- Abdominal pain: colicky in nature, associated with nausea, vomiting, bloody diarrhoea, intussusception and perforation. Due to vasculitis, bowel is oedematous and inflamed causing bleeding and obstruction. May be confused with acute surgical condition.
- Renal disease: In 30 to 70% cases, present with haematuria and proteinuria. Usually mild. Focal necrotizing glomerulonephritis, rarely renal failure may occur. In adults, 25% cases develop severe crescentic or rapidly progressing glomerulonephritis and renal failure (which are less in children).



Arthritis in Henoch-Schönlein purpura



Henoch-Schönlein purpura (buttock)

Q: What **investigations** should be done in HSP?

A: As follows:

- CBC and platelet (non-thrombocytopenic purpura).
- Urine (proteinuria and haematuria).
- Serum IgA is high in 50% cases (IgA-containing immune complex is also high).
- Skin biopsy from normal and involved skin (it will show leucocytoclastic vasculitis with deposition of IgA and complement C3 in blood vessels).
- Renal biopsy.

Q: Suggest two **investigations** that are helpful for **diagnosis**.

A: As follows:

- Serum IgA is high in 50% cases (IgA-containing immune complex is also high).
- Skin biopsy from normal and involved skin (vasculitis with deposition of IgA and complement C3 in blood vessels).

Q: Suggest one **investigation** that is helpful for **prognosis**.

A: Renal biopsy: It shows focal and segmental proliferative glomerulonephritis, sometimes with mesangial hypercellularity. In more severe cases, epithelial crescents may be present causing rapidly progressing glomerulonephritis and renal failure. This is less in children. There is IgA deposition within and around blood vessels, glomerular mesangium (it may be confused with IgA nephropathy).

Prognosis of HSP is related to the severity of renal involvement.

Q: How to **treat**?

A: As follows:

- It is self-limiting, spontaneous cure in majority of cases.
- Steroid is indicated, if GIT and joint symptoms. Steroid does not affect the course and progression of disease. Abdominal pain may be improved in 24 hours.
- In renal involvement: pulse IV steroid and cytotoxic drugs should be given.
- Recurrence may occur. Dapsone may help in cutaneous recurrence.

Q: What is the prognosis?

A: Good in children, relatively bad in adults. Adverse factors in adults are hypertension, abnormal renal function and proteinuria >1.5 g/day. But only 1% of patients develop end-stage renal failure.

Remember the following points regarding HSP in children and in adults:

In adults, features are:

- Skin involvement is common (70%).
- Gut and joint involvement occurs in 20% cases.
- Renal involvement is more common than children.
- Myocardial involvement may occur rarely.
- Prognosis is worse in adults than children.

In children, features are:

- Gastrointestinal vasculitis is more common.
- Renal and skin involvement is less common.
- Prognosis is better.

SPLENOMEGALY (HEREDITARY HAEMOLYTIC ANAEMIA)

Instruction by the examiner:

- Examine the abdomen and relevant.
- Palpate the abdomen. What are your findings (splenomegaly)? What relevant do you like to see?

Presentation of a Case: The Patient is usually of Young or Early Age.

- Spleen is hugely enlarged, . . . cm from costal margin in anterior axillary line towards right iliac fossa.

My diagnosis is **Huge splenomegaly**.

Q: What are the **causes of splenomegaly** in this young patient?

A: As follows:

- Kala-azar.
- Malaria.
- Hereditary haemolytic anaemia.
- Lymphoma.
- CLD with portal hypertension (causes are Wilson's disease and α_1 -antitrypsin deficiency).

Q: What **relevant physical findings** will you see in hereditary haemolytic anaemia?

A: As follows:

- Anaemia and jaundice.
- Frontal and parietal bossing.
- Mongoloid facies with prominent malar bones.
- Short stature.
- Also, I would like to take the family history of hereditary haemolytic anaemia.



Short stature



Parietal bossing



Malar prominence
with Pigmentation
and jaundice



Mongoloid facies

Q: What hereditary haemolytic anaemia this can be?

A: β -Thalassaemia major, HbE disease, β -thalassaemia HbE disease (double heterozygous), hereditary spherocytosis.

Q: What are the typical features of haemolytic anaemia?

A: Triad of haemolytic anaemia are:

- Anaemia.
- Jaundice.
- Splenomegaly.

Q: Mention one simple investigation that will help your diagnosis.

A: Peripheral blood film, which shows microcytic hypochromic anaemia.

Q: What are the causes of microcytic hypochromic anaemia?

A: As follows:

- Iron-deficiency anaemia (the commonest cause).
- β -Thalassaemia (major and minor).
- Sideroblastic anaemia.
- Anaemia of chronic disease.

Q: How will you confirm your diagnosis?

A: Haemoglobin electrophoresis.

Q: Mention another investigation helpful for your diagnosis.

A: Reticulocyte count (by supravital stain)—high.

Q: What investigations do you suggest?

A: As follows:

1. CBC with PBF (shows microcytic hypochromic blood picture, marked anisocytosis, poikilocytosis and target).
2. Reticulocyte count (by supravital stain)—high.
3. Haemoglobin electrophoresis.
4. Others:
 - X-ray of skull, hand and other skeletal survey.
 - Serum bilirubin: High (also urinary urobilinogen is high).
 - Serum iron profile: Ferritin (may be high, if haemosiderosis), iron (high), TIBC (reduced).

Q: What are the findings in thalassaemia in Hb-electrophoresis?

A: As follows:

- β -Thalassaemia major: Hb-F is high.
- β -Thalassaemia minor: Hb-A₂ is high.

Q: What are the radiological findings in skull in β -thalassaemia major?

A: As follows:

- Widening of diploic space.
- Thinning of outer table.
- Thickening and coarsening of trabeculae, giving rise to hair on end appearance.

READ THE FOLLOWING TOPICS IN RELATION TO THALASSAEMIA

Q: What is thalassaemia?

A: It is an inherited disorder in which there is impairment of haemoglobin production due to partial or complete failure to synthesize the specific type of globin chain (structure of globin chain is normal). 2 types:

1. β -Thalassaemia: There is inadequate production of β -chain, causing less or no production of HbA. It is of 3 types:
 - β -Thalassaemia major: HbA is less, HbF is more.
 - β -Thalassaemia minor: HbA₂ is increased.
2. α -Thalassaemia: There is an inadequate production of α -chain, so less HbA, HbF and HbA₂ as all of them contain α -chain.
3. Thalassaemia intermedia, characterized by the combination of homozygous mild β -thalassaemia plus α -thalassaemia. It is usually less severe and does not require blood transfusion as anaemia is mild to moderate.

Q: How to treat β -thalassaemia major?

A: As follows:

1. Correction of anaemia: Blood transfusion to keep Hb% above 10 gm%, every 4 months (life span of RBC is 4 months).
2. Folic acid 5 mg daily, to be continued.
3. Iron containing drugs and diet are avoided (iron can only be given if there is deficiency).
4. Repeated blood transfusion may cause haemosiderosis. It can be prevented by chelating agent, desferrioxamine subcutaneously (1.5 to 2 g with each unit of blood) in the anterior abdominal wall with infusion pump for 12 hours. It may also be given with infusion drip (normal saline or aqua). Vitamin C 200 mg daily may be added (it causes urinary excretion of iron). Oral iron chelating agents such as deferiprone (75 mg/kg in 2 to 4 divided doses) or deferasirox may be used.
5. Other treatment:
 - Injection erythropoietin. It stimulates bone marrow and increases normal haemoglobin to some extent.
 - Hydroxyurea 1 to 2 gm daily may be helpful (it prevents ineffective erythropoiesis).
6. Specific therapy:
 - Allogenic bone marrow transplantation from HLA compatible sibling. Haematological cure is >90%. When transplantation is done before development of hepatomegaly or portal HTN.
 - Also, gene therapy.
7. Splenectomy (in some cases).
8. Genetic counselling should be offered. It is necessary for prenatal diagnosis.

Q: What are the indications of splenectomy?

A: As follows:

- Hypersplenism: As suggested by repeated transfusion in a short interval. CBC shows pancytopenia.
- Huge splenomegaly with pressure symptoms.
- Blood transfusion requirement is >200 ml/kg/year of packed cell.

Q: What should be done before and after splenectomy?**A:** As follows:

Precondition for splenectomy:

- Age >5 years (because of immune system maturity).
- Vaccination against pneumococcus, meningococcus, *H. influenzae* type-b (4 weeks prior to surgery).

Care after splenectomy:

- Annual influenza vaccine.
- Pneumococcal polysaccharide 2 months after initial vaccination.
- Pneumococcal vaccine repeated every 5 years after initial vaccine.
- Quadravalent meningococcal/diphtheria conjugate and meningococcal polysaccharide every 5 years.
- Long term penicillin V 250 mg 12 hourly (erythromycin in penicillin allergy).
- Meningococcal polysaccharide vaccine (ACWY) for travellers to Africa/Saudi Arabia, e.g., during Hajj and Umrah.

Q: What are the complications of repeated blood transfusion?**A:** As follows:

- Repeated transfusion may cause haemosiderosis (usually when more than 30 to 50 L of blood is transfused).
- Infections such as hepatitis B, C, D and HIV.

Q: If the patient develops severe abdominal pain, what are the likely causes?**A:** As follows:

- Cholelithiasis (usually pigment stone, due to haemolysis).
- Also splenic infarction and acute pancreatitis.

Q: When anaemia develops in a patient with thalassaemia major after delivery?**A:** Anaemia develops at the age of 4 to 6 months. Normally, HbF disappears 4 to 6 months after birth. In adults, HbF is <1%. But in thalassaemia major, HbF is high.**Q: How can it be diagnosed before birth?****A:** Prenatal diagnosis is possible by obtaining chorionic villus material for DNA. It should be done if both parents suffer from β -thalassaemia minor. If β thalassaemia is found in the foetus, then termination of pregnancy is indicated.**Q: What are the presentations of thalassaemia minor? What is the differential diagnosis? How to treat?****A:** As follows:

- Usually asymptomatic. Incidentally diagnosed during blood count, microcytic hypochromic blood picture.
- There may be features of anaemia (microcytic hypochromic).
- Haemoglobin electrophoresis shows high HbA₂.

Differential diagnosis of thalassaemia minor: Iron deficiency anaemia (IDA).

Treatment: In asymptomatic case, no treatment needed, only follow-up.

Q: How to **differentiate** thalassaemia from IDA?

A: Thalassaemia minor confuses with iron deficiency anaemia. Main differences are:

- Anaemia is more marked in iron deficiency and relatively less in thalassaemia minor.
- Also, in iron deficiency, there is low iron, low ferritin and high total iron binding capacity.

Q: What are the **complications** of thalassaemia major?

A: As follows:

- Growth retardation.
- Bony deformity such as frontal, parietal bossing.
- Recurrent infection.
- Spinal cord compression (due to extra-medullary haemopoiesis).
- Complication of repeated transfusion: haemosiderosis, infection with HBV, HCV, HIV.

Q: If a thalassaemia major patient develops **paraplegia**, what may be the cause? How will you **treat**?

A: Spinal cord compression due to extra-medullary haemopoiesis. Radiotherapy to the spine may be given to relieve compression.

ANAEMIA (IRON DEFICIENCY ANAEMIA)

Instruction by the examiner:

- Perform the general examination.

Presentation of a Case:

- The patient is pale, moderately anaemic.

My diagnosis is **Anaemia**.

Q: What is the **commonest** anaemia?

A: Iron deficiency anaemia.

Q: What **simple investigation** is done to diagnose iron deficiency anaemia?

A: Peripheral blood film (shows microcytic, hypochromic blood picture).

Q: What **history** would you take in iron deficiency anaemia?

A: As follows:

- Bleeding from any site (haemorrhoid, haematemesis, melaena, gum bleeding, any bleeding disorder, injury).
- In female (menorrhagia and repeated pregnancy).
- Drugs (NSAID in patient with arthritis).
- History of malabsorption.
- Less intake of food (anorexia, dysphagia and poverty).
- Chronic illness (e.g., malignancy).

Q: Tell **one peculiar symptom** in iron deficiency anaemia.

A: Pica. It means eating of unusual items such as earth, coal, ice or some foods in excess like tomato, sour foods. The cause is unknown.

Q: What are the **causes** of iron deficiency anaemia?

A: As follows:

- Bleeding due to any cause: Commonest from gastrointestinal tract (haemorrhoid, colorectal carcinoma, carcinoma stomach, diverticulitis, angiodysplasia), menorrhagia in female.
- Hookworm (also schistosomiasis).
- Less intake of food.
- Malabsorption.
- More demand (pregnancy).

Q: What is the **daily requirement** of iron?

A: 1.0 mg/day. But in pregnancy, extra 2.5 mg/day is needed (hence total 3.5 mg/day is required). Normal daily intake is 15 to 20 mg, only 10% is absorbed. But absorption increases in iron deficiency and pregnancy.

Q: What investigations are done in iron deficiency anaemia?**A:** As follows:

1. Test to confirm iron deficiency anaemia:
 - CBC with PBF (shows microcytic hypochromic blood picture).
 - Serum iron, TIBC and ferritin (shows low iron, increased TIBC and low ferritin).
2. Test to find out the causes (according to the history and suspicion of cause):
 - Stool for ova or cyst of hookworm, occult blood test.
 - Endoscopy (to see oesophageal varices, peptic ulcer, polyp, telangiectasia, carcinoma stomach).
 - Proctoscopy (to see haemorrhoid),
 - Sigmoidoscopy or colonoscopy (to see neoplasm, polyp, diverticulum, ulcer, angiodysplasia of colon).
 - USG of abdomen (any mass, fibroid uterus).
3. Bone marrow to see stainable iron (by Prussian blue shows empty stain): **not a routine**, may be done in some cases.

Q: What are the causes of microcytic hypochromic blood picture?**A:** As follows:

- Iron deficiency anaemia (commonest).
- Thalassaemia.
- Sideroblastic anaemia.
- Anaemia of chronic disorder.

Q: What are the features of iron deficiency anaemia?

A: Common symptoms of anaemia with brittle nails, spoon shaped nails (koilonychia), atrophy of the papillae of the tongue, angular stomatitis, brittle hair, a syndrome of dysphagia and glossitis (Plummer Vinson or Paterson Brown Kelly syndrome).

Q: How to treat iron deficiency anaemia? How long will you continue the treatment?**A:** As follows:

- If severe anaemia or haemoglobin is low: blood transfusion (packed cell).
- Iron therapy: Oral ferrous sulphate (200 mg 8 hourly), ferrous gluconate (300 mg 12 hourly) or ferrous fumarate. To be given for 3 to 6 months after haemoglobin is normal to replenish the iron store.
- Delayed release preparation of iron is not helpful, as they release iron beyond the upper small intestine, where it cannot be absorbed.
- If the patient is unable to take orally, or malabsorption or IBD, parenteral iron therapy should be given.
- Treatment of cause should be done (e.g., menorrhagia, haemorrhoid etc.).

Q: How to see the response to iron therapy?**A:** Increase in reticulocytes after 1 week.

READ THE FOLLOWING TOPICS IN RELATION TO ANAEMIA

Q: What is anaemia? What are the types?

A: Anaemia may be defined as a clinical condition, characterized by reduced level of haemoglobin according to the age and sex of the individual. It may be classified in 2 ways: Aetiological (based on cause) and morphological (based on morphology of RBC).

Aetiological:

1. Haemorrhagic anaemia (due to blood loss). Causes are:
 - Acute: Trauma, postpartum bleeding, haematemesis, melaena, epistaxis.
 - Chronic: Hook worms, haemorrhoids, excessive menstrual loss, bleeding peptic ulcer etc.
2. Dyshaemopoietic anaemia (due to inadequate production of RBC). Causes are:
 - Deficiency anaemia: Iron, vitamin B₁₂, folate deficiency.
 - Aplastic anaemia (bone marrow failure, which may be primary or secondary to some other diseases or drugs).
 - Anaemia of chronic disorder. Cause are: SLE, rheumatoid arthritis, CKD.
 - Others: Hypothyroidism, sideroblastic anaemia, malignancy.
3. Haemolytic anaemia. Causes are:
 - Genetic: Red cell membrane defect (e.g., hereditary spherocytosis, eliptocytosis, stomatocytosis), haemoglobin abnormality (thalassaemia, sickle cell anaemia) or enzyme defects (G6PD deficiency, pyruvate kinase deficiency).
 - Acquired: Autoimmune, toxic, mechanical and infectious causes.

Morphological (depending on MCV and MCHC). 4 types:

1. Normocytic normochromic anaemia (normal MCV and MCHC).
2. Microcytic hypochromic anaemia (low MCV <76 fl, low MCHC <30 g/dL).
3. Macrocytic anaemia (high MCV >96 fl).
4. Dimorphic anaemia (2 cell lines: Macrocytes and microcytes).

Q: What are the causes of normocytic normochromic anaemia?

A: As follows:

- Anaemia of chronic disorder.
- Chronic infection (e.g., tuberculosis).
- Collagen disease (e.g., SLE, RA).
- Malignancy.
- Endocrine disease.
- Sideroblastic anaemia.

Q: What are the causes of microcytic hypochromic anaemia?

A: (See above).

Q: What are the causes or mechanisms of anaemia of chronic disorder?

A: Actual mechanism is unknown. It is due to abnormality of iron metabolism and erythropoiesis. There is less erythropoietin. Also, red cell survival is short.

Q: What are the causes of macrocytic anaemia?**A:** As follows:

1. Macrocytosis with megaloblastic marrow are found in:
 - Vitamin B₁₂ deficiency.
 - Folic acid deficiency.
2. Macrocytosis with normoblastic marrow are found in:
 - Chronic liver disease.
 - Chronic alcoholism.
 - Hypothyroidism.
 - Haemorrhage.
 - Haemolysis.
 - Others: Sideroblastic anaemia, pure red cell aplasia, azathioprine therapy.

Q: What is dimorphic anaemia? What are the causes?**A:** When both microcytes and macrocytes are found, this is called dimorphic anaemia. Causes are:

- Combined iron, B₁₂ and folate deficiency.
- Sideroblastic anaemia.
- Treatment of anaemia.

Q: What are the signs that indicate to a specific cause of anaemia?**A:** As follows:

Sign	Cause of Anaemia
1. Triad of anaemia, jaundice and splenomegaly	1. Haemolytic anaemia
2. Angular cheilitis, glossitis, koilonychia	2. Iron deficiency anaemia
3. Glossitis	3. Iron deficiency anaemia, vitamin B12 or folate deficiency
4. Splenomegaly	4. Malaria, chronic haemolytic anaemia, acute infection, leukaemia, lymphoma, portal hypertension
5. Neurological changes (dementia, optic atrophy and features of subacute combined degeneration of spinal cord) and lemon yellow tint.	5. Vitamin B12 deficiency (megaloblastic anaemia).
6. Bony change (frontal and parietal bossing)	6. Hereditary haemolytic anaemia
7. Leg ulcer	7. Sickle cell anaemia, paroxysmal nocturnal haemoglobinuria
8. Bony tenderness	8. Acute leukaemia, multiple myeloma, lymphoma, myelofibrosis

Q: How to investigate a patient with anaemia?**A:** Detailed history, physical examination and relevant laboratory investigations are done to diagnose anaemia.

History of the patient:

- Dietary history (to diagnose deficiency such as iron, vitamin B₁₂ and folic acid deficiency).
- Less intake of food (due to anorexia, anorexia nervosa or any primary disease).
- Malabsorption.
- History of bleeding (haemorrhoid, epistaxis, haematemesis, melaena, menorrhagia in female etc.).
- In female: Multiple pregnancies, repeated abortion.
- Drug history: NSAID, steroid, drugs causing bone marrow suppression (e.g., cytotoxic drugs), drugs causing haemolysis (e.g., sulfasalazine, methyldopa etc.).
- History of surgery: Gastrectomy or partial gastrectomy, ileal surgery (responsible for vitamin B₁₂ absorption).
- Family history (in hereditary haemolytic anaemia).
- History of any chronic disease (e.g., SLE, CRF, CLD, malignancy etc.).

Clinical examination: See page 491.

Laboratory investigations:**1. CBC with PBF:**

- Pancytopenia: May be due to aplastic anaemia, hypersplenism, megaloblastic anaemia, aleukaemic leukaemia.
- PBF: May be normocytic, microcytic, macrocytic or dimorphic (see below).
- Reticulocyte count: High in haemolytic anaemia.
- MCV and MCHC.

2. Bone marrow examination: To diagnose megaloblastic anaemia, aplastic anaemia, bone marrow infiltration (secondary deposit), ring sideroblasts (in sideroblastic anaemia).

3. Other investigations according to suspicion of cause.

Further investigation of microcytic hypochromic anaemia (low MCV and low MCHC):

- For iron deficiency anaemia: Serum iron, TIBC, serum ferritin.
- For hereditary haemolytic anaemia: Haemoglobin electrophoresis, skeletal survey.
- For sideroblastic anaemia: According to history, bone marrow examination (ring sideroblasts)
- For anaemia of chronic disease: According to history of the patient.

Further investigations for macrocytic anaemia (high MCV):

- Bone marrow study is done. If megaloblast seen, serum B₁₂ and folic acid assay should be done. If normoblast is found, further investigation should be done according to history (see above).

Q: What is pernicious anaemia?

A: It is an autoimmune disease, in which, there is atrophy of gastric mucosa with loss of parietal cells causing intrinsic factor deficiency. So, vitamin B₁₂ is not absorbed. There is anti-intrinsic factor (50%) and anti-parietal cell antibodies (90%) in the blood. In the absence of intrinsic factor, less than 1% of dietary vitamin B₁₂ is absorbed.

It is common in elderly, average age of onset is 60 years, more in female. There is a higher incidence of gastric carcinoma with PA (1 to 3%) than in the general population.

It is more common in individuals with other autoimmune disease (Hashimoto's thyroiditis, Graves' disease, vitiligo, hypoparathyroidism or Addison's disease) or a family history of these or pernicious anaemia.

Q: How to treat pernicious anaemia?

A: Vitamin B12 deficiency is treated with hydroxycobalamin 1000 µg IM for 6 doses 2 or 3 days apart, followed by maintenance therapy of 1000 µg every 3 months for life.

Q: What is spurious anaemia?

A: When plasma volume is increased and haemoglobin is relatively low, it is called spurious anaemia. It is found in pregnancy.

Q: What is spurious polycythaemia?

A: Here haemoglobin is relatively increased due to low plasma volume. This is found in dehydration.

Q: What is sideroblastic anaemia?

A: Sideroblastic anaemias are inherited or acquired disorders characterized by refractory anaemia, a variable number of hypochromic cells in the peripheral blood with excess iron and ring sideroblasts. Blood film usually shows microcytic anaemia, may be dimorphic.

Classification:**1. Hereditary:**

- X-linked disease, transmitted by female.

2. Acquired:

- Primary (one of the myelodysplastic syndromes).
- Secondary:
 - Inflammatory: Rheumatoid arthritis.
 - Neoplastic: Lymphoma, leukaemia, carcinoma, myeloproliferative disorders, multiple myeloma, carcinoma.
 - Drugs: Isoniazid, pyrazinamide, ciclosporine.
 - Alcohol abuse.
 - Lead poisoning.
 - Other disorders, e.g., megaloblastic and haemolytic anaemias, malabsorption, severe malnutrition, erythroleukaemia.

Treatment:

- Treatment of primary cause, if present, e.g., withdrawal of drug, stop alcohol intake etc.
- Some cases may respond to pyridoxine, folic acid.
- Correction of anaemia by blood transfusion.

Q: What is ring sideroblast?

A: It is characterized by accumulation of iron in mitochondria of erythroblast around the nucleus, giving a ring shaped appearance in the bone marrow.

Q: What diseases may be diagnosed from PBF?**A:** As follows:

Finding	Description	Common Causes
1. Anisocytosis	Variation in size of RBC	Iron deficiency anaemia, megaloblastic anaemia, sideroblastic anaemia
2. Poikilocytosis	Variation in shape of RBC	Iron deficiency anaemia, thalassaemia, sideroblastic anaemia
3. Microcytosis	MCV <76 fL	Iron deficiency anaemia, thalassaemia, sideroblastic anaemia, anaemia of chronic disorder
4. Macrocytosis	MCV >96 fL	Vitamin B12 and folic acid deficiency, chronic liver disease, alcohol, hypothyroidism, zidovudine
5. Hypochromia	Central pallor of RBC is more (lower haemoglobin content)	Iron deficiency anaemia, thalassaemia, sideroblastic anaemia, anaemia of chronic disorder
6. Basophilic stippling or punctuate basophilia	Deep blue dots scattered in cytoplasm of RBC (seen with Romanowsky staining)	Chronic lead poisoning, dyshaemopoiesis
7. Target cells	Flat red cells with a central mass of haemoglobin (dense area) surrounded by a ring of pallor (pale area) and an outer ring of haemoglobin (dense area)	Iron deficiency anaemia, thalassaemia, Hb C disease, CLD, splenectomy
8. Howell-Jolly bodies	Small, round remnants of nuclear material in RBC. These are normally removed by spleen.	Hyposplenism, post-splenectomy, dyshaemopoiesis
9. Heinz bodies (Ehrlich's bodies)	Formed from denatured, aggregated haemoglobin in RBCs (seen with supravital staining with brilliant cresyl blue).	Thalassaemia, haemolysis in glucose-6-phosphate dehydrogenase deficiency, asplenia and CLD, drug (sulfasalazine, dapsone)
10. Acanthocytes (spur cells)	RBC with irregular spicules	Abetalipoproteinaemia
11. Burr cells	RBC with regularly placed spicules	CKD
12. Schistocytes	Fragmented RBC. These are found in microangiopathic haemolytic anaemia.	Causes: DIC, haemolytic uraemic syndrome (HUS), TTP, disseminated carcinomatosis, malignant or pregnancy induced hypertension (eclampsia)
13. Spherocytes	Small, densely packed RBC with loss of central pallor	Hereditary spherocytosis, autoimmune haemolytic anaemia, postsplenectomy
14. Sick cell	Sickle shaped	Sickle cell anaemia
15. Blister cells	RBC containing peripheral vacuole.	Glucose-6-phosphate dehydrogenase deficiency
16. Nucleated RBC	Normoblasts	Bone marrow infiltration, severe haemolysis, myelofibrosis, acute haemorrhage
17. Polychromatia	Young red cells, reticulocytes (bluish tinge)	Haemolysis, acute haemorrhage, increased red cell turnover

SPLENOMEGALY (DISCUSSION ABOUT POLYCYTHAEMIA RUBRA VERA)

Instruction by the examiner:

- Examine the abdomen and see the relevant.
- Look at the face and palpate the abdomen.

Presentation of a Case: (Patient is usually Young, Face is Plethoric)

- Spleen is enlarged, . . . cm from costal margin in anterior axillary line towards right iliac fossa.

Q: What are the **causes** of splenomegaly?

A: Mention as described previously (in splenomegaly).

Q: Look at the face and ask **one question** in this patient.

A: Face is plethoric, deep dusky, cyanosed, redness of conjunctiva (bloodshot eyes). I would like to ask whether any history of itching, especially after hot bath or warm body.

Q: What is your **diagnosis** in this case?

A: Polycythaemia rubra vera (PRV).

Q: What are the **features** of PRV?

A: PRV is common in males, after 40 years. Features are:

Symptoms:

- Features of hyperviscosity syndrome: headache, dizziness, giddiness, blackout, lack of concentration, blurring of vision.
- Pruritus after hot bath or with warm body.
- Peptic ulcer is common, bleeding may occur.
- Heaviness in the left upper abdomen (due to splenomegaly).
- Thrombosis (CVD, peripheral vascular disease), intermittent claudication, hypertension, angina.

Signs:

- Face—plethoric, deep dusky, cyanosed, redness of conjunctiva (bloodshot eyes).
- Splenomegaly (70%), hepatomegaly (50%).
- Fundoscopy: engorged retinal vessels.
- Hypertension.

NB: *Plethoric appearance, splenomegaly, increased RBC, WBC and platelets are highly suggestive of PRV.*

Q: What are the findings of **fundoscopy**?

A: Engorged retinal vessels, may be bleeding.

Q: What investigations are done in PRV?**A:** As follows:

- CBC, platelet count, ESR (high haemoglobin, RBC, WBC, platelet, basophil. ESR is low).
- Haematocrit or Packed cell volume (PCV): high, 65% (normal up to 45%).
- Red cell mass measured with radioactive ^{51}Cr labelled red cells (increased).
- Erythropoietin is low or absent (high in secondary polycythaemia).
- Bone marrow shows erythroid hyperplasia and increased megakaryocyte.
- *JAK-2* mutation present (negative in some cases).
- Others: high LAP score, high vitamin B_{12} , high uric acid.

N.B.: High haematocrit and the presence of the JAK-2 mutation are highly suggestive of PRV. In JAK-2 negative cases, high red cell mass with absence of other causes of secondary erythrocytosis is diagnostic.

Q: What are the causes of polycythaemia?**A:** It may be of 2 types. Absolute and relative. Absolute may be primary or secondary.**Primary polycythaemia:**

- Polycythaemia rubra vera

Secondary polycythaemia:

1. Physiological: High altitude.
2. Respiratory cause: COPD, chronic bronchitis, emphysema, Obstructive sleep apnoea.
3. Smoking.
4. Cardiac: Cyanotic congenital heart disease (TOF),
5. Pathological erythropoietin production
 - Tumours—renal cell cancer, cerebellar haemangioblastoma, hepatoma, pheochromocytoma, uterine fibroid.
 - Drug associated—Erythropoietin administration.

Q: What is relative polycythaemia?**A:** It is the polycythaemia secondary to reduced plasma volume. Causes are—dehydration, diuretic, smoking, alcohol excess, obesity, Gaisbock's syndrome.**Q: What is Polycythaemia rubra vera (PRV)?****A:** Polycythaemia rubra vera is a stem cell disorder in which there is excess proliferation of erythroid, myeloid and megakaryocyte progenitor cells.**Q: How to differentiate PRV from secondary polycythaemia?****A:** In PRV, Red cell mass is increased and erythropoietin is low or absent. But in secondary polycythaemia, red cell mass is low and erythropoietin is normal or high.

Q: What are the **diagnostic criteria** of PRV?

A: As follows (WHO criteria):

Major criteria:		
1. Haemoglobin • >16.5 g/dL in men • >16 g/dL in women	Or, haematocrit • >49% in men • >48% in women	Or, increased red cell mass (>25% of normal)
2. Bone marrow showing hypercellularity with erythroid, granulocytic and megakaryocytic proliferation with pleomorphic, mature megakaryocytes (differences in size)		
3. Presence of <i>JAK2</i> V617 F or <i>JAK2</i> exon 12 mutation		
Minor criteria:		
1. Serum erythropoietin level below the reference range for normal		
<i>Diagnosis of PRV requires either all three major criteria or the first two major criteria and the minor criterion</i>		

Q: Suggest one **investigation**.

A: Measurement of red cell mass (increased).

Q: Suggest one **treatment**.

A: Venesection (400 to 500 mL of blood, every 5 to 7 days) until haematocrit is <45% and platelet <400 × 10⁹/L).

N.B.: Regular venesection may cause iron deficiency (but iron therapy should be avoided).

Q: What are the treatments of PRV?

A: As follows:

- Venesection.
- Radioactive phosphorus for elderly (5 mCi of ³²P IV). It may cause acute leukaemia.
- Other drugs—hydroxyurea, α interferon may be given.
- Low dose intermittent busulphan may be used. It may cause acute leukaemia.
- Aspirin reduces risk of thrombosis.
- Allopurinol (if uric acid is high).
- Anagrelide: inhibits megakaryocyte differentiation and is useful for thrombocytosis.

Q: What is the **prognosis** in PRV?

A: Median survival—10 years, some 20 years.

Q: What are the complications of PRV?

A: As follows:

- Myelofibrosis (15%)
- Acute myeloid leukaemia
- Refractory state with anaemia.
- Thromboembolism (cerebral, coronary).
- Hypertension.
- Angina.
- Intermittent claudication.
- Bleeding tendency.
- Gout.
- Peptic ulcer.

SPLENOMEGALY (MYELOFIBROSIS)

Instruction by the examiner:

- Examine the abdomen, Or, palpate the abdomen.

Presentation of a Case: The Patient is usually Middle-Aged or Elderly.

- Spleen is hugely enlarged, . . . cm from costal margin in anterior axillary line towards right iliac fossa.

Q: What are the **causes of splenomegaly** in this middle aged patient?

A: Mention as described previously (in splenomegaly).

Q: What is **myelofibrosis** and how does the patient usually **present**?

A: Myelofibrosis is a disorder of unknown cause characterized by clonal proliferation of the stem cells with bone marrow fibrosis, extramedullary haemopoiesis and leucoerythroblastic blood picture. Fibrosis in the marrow is due to hyperplasia of abnormal megakaryocyte, which releases fibroblast stimulating factors such as platelet derived growth factor.

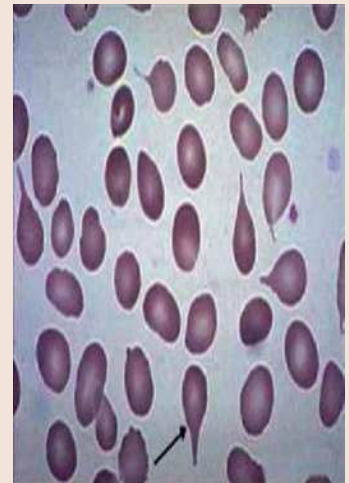
It is common above 50 years. History of polycythaemia rubra vera is found in 25% cases and 50% have *JAK-2* mutation seen in polycythaemia rubra vera. Features are:

- May be asymptomatic. Mass in the left hypochondrium or hepatosplenomegaly.
- General features of malaise, weakness, loss of weight, night sweat, repeated infection and bleeding.
- There may be peptic ulcer, pruritus after hot bath and gout.

Q: What investigations do you suggest?

A: As follows:

1. CBC and PBF:
 - Leucocytosis, leucoerythroblastic blood picture in which there are premature cells of WBC (myelocytes and myeloblast) and RBC series (reticulocyte and immature nucleated RBC). Though initially there is leucocytosis, later there may be leucopenia.
 - PBF shows tear drop RBC (tear drop poikilocytes).
 - Platelets are very high and later decreased. Giant forms may be seen.
 - Anaemia is usually macrocytic and pancytopenia may occur.
2. Bone marrow may be dry tap, trephine biopsy should be done (which shows increased megakaryocyte, increased reticulin and fibrous tissue).
3. Others: leucocyte alkaline phosphatase (LAP) score is increased, uric acid is high and folic acid is low.
4. Genetic test may show *JAK-2* mutation. *CALR* mutation may be present in *JAK-2* negative case.



Tear drop poikilocyte

Q: How to **treat** of myelofibrosis?**A:** As follows:

- Correction of anaemia by blood transfusion and folic acid.
- Hydroxyurea (it reduces WBC and splenomegaly).
- Radiotherapy for huge spleen.
- Allopurinol, Febuxostat may be used if uric acid is high.
- Ruxolitinib (JAK-2 inhibitor) may be used. It does not eradicate the disease but improves life expectancy.
- Splenectomy, if huge spleen with pressure symptoms and features of hypersplenism.
- Allogenic bone marrow transplantation or HSCT (haematopoietic stem cell transplantation), if the patient is young.

Prognosis: Median survival is 4 years (ranges from 1 to 20 years).

Q: What are the **causes of death** in myelofibrosis?**A:** As follows:

- Transformation to AML (10 to 20%).
- Infection.
- Bleeding (from GIT).
- Cardiovascular problem.

Q: How to **differentiate myelofibrosis** from CML?**A:** As follows:

- Marrow finding.
- Philadelphia chromosome (absent in myelofibrosis).
- LAP score (increases in myelofibrosis and decreases in CML).
- In CML, WBC count is very high with precursors of granulocytes, which are absent in myelofibrosis.

ENDOCRINOLOGY

6

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ENDOCRINOLOGY

6

'You see, but you do not observe'
—Sir Arthur Conan Doyle

It is quite common that one may get a case related to endocrine disorders, more frequently thyroid disorders, although other diseases are also not rare.

Remember, the diagnosis of endocrine disease may be obvious by looking at the patient. Once you are asked to examine the patient, take few seconds to have a quick look from head to foot carefully. Diagnosis of thyroid disorders (such as Graves' disease, thyrotoxicosis, hypothyroidism) is obvious on the face of the patient. Also, Cushing's syndrome and acromegaly are easily diagnosed by looking at the patient.

Many a times, examiner used to ask:

- 'Look at the face. What is your diagnosis? What else do you want to examine?'
- 'Examine the neck of this patient.'
- 'Perform the general examination'.
- 'Examine the hands of this patient'.

Underlying diagnoses by looking at the face may be:

- Graves' disease (hyperthyroid, euthyroid or hypothyroid) or thyrotoxicosis (due to any cause).
- Hypothyroidism (myxoedema).
- Cushing's syndrome.
- Acromegaly.
- Pigmentation (in Addison's disease).

Subsequent physical examination depends on your diagnosis. For example (for details, see later in this chapter):

- If your diagnosis is thyroid disease: further clinical examination will be related to thyroid problems, e.g., signs of thyrotoxicosis, signs of hypothyroidism, examination of the eye, thyroid gland etc.
- If your diagnosis is Cushing's syndrome: examine other findings in relation to this (central obesity, striae, proximal myopathy, blood pressure).
- If acromegaly is suspected: then examine the face, hand, visual field, voice.

After you have observed the patient, the examiner may ask, 'What is the likely diagnosis? Ask some questions to the patient'. In such a case, you must have few **readymade questions** to be asked in a particular disease. For example:

- If Cushing's syndrome is suspected: ask whether the patient is taking steroid for long time, or experiencing weight gain, backache, difficulty in standing up after sitting etc.

- If hypothyroidism is suspected: ask whether the patient has cold intolerance, weight gain, increased sleep, constipation. Also, while talking to the patient, observe any voice change.
- If hyperthyroidism is suspected: ask whether the patient prefers cold, excessive sweating, increased appetite but weight loss, irritability.
- If acromegaly is suspected: ask the patient, whether patient's body size has increased, visual disturbance, weight gain and weakness, history of previous surgery (pituitary), also observe the voice.
- If the patient is emaciated: ask about features of diabetes mellitus (polyuria, polydipsia), thyrotoxicosis, Addison's disease, panhypopituitarism.

Common short cases may be:

- Simple goitre (single or multinodular or diffuse).
- Toxic goitre (single or multinodular).
- Myxoedema.
- Grave's disease.
- Exophthalmos.
- Acromegaly.
- Tall stature/ Gigantism.
- Short stature.
- Addison's disease.
- Complications of DM (retinopathy, neuropathy, diabetic foot).

EXAMINATION OF THYROID GLAND

Instruction by the examiner:

- Examine the thyroid gland or examine the neck.
- Examine the thyroid status of this patient (look for **signs of thyrotoxicosis** and also **signs of hypothyroidism**).
- Look at the face (hypothyroid, exophthalmos). What else do you want to examine?

Proceed as follows:

1. Introduce yourself. While shaking hand, check whether the hand is warm and sweaty or cold and sweaty.
2. Look at the patient's face:
 - Anxious, restless, fidgety and frightened face with staring looks (indicates thyrotoxicosis).
 - Puffy face with periorbital swelling with baggy eyelids, loss of outer 1/3^d of eyebrows and apathetic look (indicates hypothyroidism).
 - Exophthalmos (bilateral or unilateral, may be due to Graves' disease).
 - Normal face with goitre (indicates euthyroid goitre).
3. Then look (inspection), palpate and auscultate thyroid gland.
4. Inspection: Examine the neck both in front, left and right sides.
 - Obvious swelling (goitre): Ask the patient for deglutition (offer a glass of water or juice, then ask the patient to drink it). If any goitre, see whether it is diffuse, single or multinodular, check if one side is larger than the other.
 - Skin colour (redness indicates infective thyroiditis) and any scar (due to previous surgery).
 - Other obvious swelling (such as lymphadenopathy).
5. Palpation (from back): Ask the patient to sit, ensure the neck is slightly flexed, palpate the gland with both hands and ask the patient to swallow again.

If goitre is present, see if it is unilateral or bilateral, diffuse or nodular (single or multinodular), then examine following points:

 - Size (which one is large, right or left).
 - Shape (diffuse or irregular).
 - Surface (smooth or irregular).
 - Consistency (soft or firm or hard).
 - Tenderness (if present, indicates subacute thyroiditis or infective thyroiditis).
 - Mobility.
 - Overlying skin condition.
 - Lower margin (to see retrosternal extension).
6. Examine for retrosternal extension (prominent veins in neck and upper chest, feel the lower limit, tracheal deviation and percuss the upper part of chest for dullness. Examine for Pemberton's sign, see below).
7. Palpate the cervical lymph nodes (if palpable, it may be suggestive of metastasis).
8. Feel for carotid pulse (absence of pulsation indicates pressure effect or malignant infiltration).
9. Finally, ask the patient to hold breath and auscultate for thyroid bruit (also carotid bruit and venous hum, which can be obliterated by gentle pressure at the root of neck). If thyroid bruit is present, check whether it is a murmur of aortic stenosis (ejection systolic murmur) radiating from chest.

Finally, tell the examiner, 'I want to examine the thyroid status, eyes, pretibial myxoedema and heart'. For **thyroid status**, look for the **signs of thyrotoxicosis** and **signs of hypothyroidism**.

Signs of thyrotoxicosis:

- See tremor of outstretched hands with fingers spread out. If no tremor, put a paper over the fingers, see the tremor.
- Palm: Whether warm and sweaty (in anxiety, palm is cold and sweaty).
- Pulse: Tachycardia, $>100/\text{minute}$ (better to record sleeping pulse).
- Others: Generalized wasting, proximal myopathy and exaggerated jerks.

Signs of hypothyroidism:

- Puffy face with periorbital swelling with baggy eyelids, loss of outer $1/3^{\text{rd}}$ of eyebrows and apathetic look.
- Non-pitting oedema (in leg).
- Pulse: Bradycardia ($<60/\text{minute}$).
- Speech: Hoarse, croaky or husky voice.
- Dry and thick skin.
- Slow relaxation of ankle jerk (very important single bedside test).

Q: What are the findings in the eyes?

A: Exophthalmos, lid lag, lid retraction and eye movement (see exophthalmos on page 510).

Q: What are the other physical findings to be seen?

A: Other physical findings (not related to toxicosis):

- Legs: Pretibial myxoedema (present only in Graves' disease).
- Nails: Onycholysis in Graves' disease.
- Heart: CCF (in thyrotoxicosis or hypothyroidism), AF or ectopics (in thyrotoxicosis).

Q: What is Pemberton's sign?

A: It is a sign to detect retro-sternal extension of thyroid gland (also positive with any retrosternal mass). On raising both arms above the head, the patient with retro-sternal extension may develop the following signs of compression:

- Face: Suffusion or congestion and cyanosis.
- Respiratory distress (stridor).
- Neck veins are engorged.
- The patient may complain of dizziness and may develop syncope (this sign is rare, not specific for retrosternal goitre).



Lid lag



Lid retraction



Pretibial myxoedema



Onycholysis in Graves disease

N.B. Remember the following points:

- *Eye signs (exophthalmos, periorbital oedema, chemosis and diplopia), pretibial myxoedema and thyroid acropachy are present only in Graves' disease. However, lid lag and lid retraction occurs in thyrotoxicosis, which are due to sympathetic overactivity, which supplies levator palpebrae muscle.*
- *Thyroid bruit is present in Graves' disease.*
- *Other findings in hands in thyrotoxicosis: palmar erythema, onycholysis (separation of nails from bed called Plummer sign is present only in Graves' disease) and clubbing (in thyroid acropachy—only in Graves).*
- *Exophthalmos and pretibial myxoedema do not correlate with toxicosis. It may be present both in hyper or hypo or euthyroid state associated with Graves' disease.*

Q: Show me the **features** of thyrotoxicosis. Ask some questions.

A: See the features above. Then ask history of excessive sweating or heat intolerance, history of palpitation, diarrhoea, appetite and weight loss.

Q: What are the **causes** of painful thyroiditis or thyroid swelling?

A: As follows:

- Subacute thyroiditis (De Quervain's thyroiditis).
- Radiation thyroiditis.
- Infectious thyroiditis.

Q: What are the **causes** of painless thyroiditis or thyroid swelling?

A: As follows:

- Hashimoto's thyroiditis.
- Post-partum thyroiditis.

FACE IN THYROID DISEASE (BY LOOKING AT THE FACE)

Instruction by the examiner:

- Look at the face. What is your diagnosis? What else do you want to see? (Examine the face and neck to see any goitre, whether diffuse or nodular. Look from head to foot, observe generalized swelling of the body and non-pitting oedema).

Presentation of a Case (Exophthalmos): Case No. 1

- The patient looks anxious, restless and fidgety.
- There is bilateral or unilateral exophthalmos (mention accordingly).
- Thyroid gland is diffusely enlarged.

Diagnosis is **Graves' disease** with thyrotoxicosis.

Q: What else do you like to see?

A: I want to see the signs of thyrotoxicosis. Also, I want to examine the thyroid gland, eyes and legs (page 512).



Case 1: Graves disease



Case 2: Myxoedema
(non-goitrous)



Case 3: Graves disease
(hypothyroid)



Case 4: Myxoedema
(goitrous, Hashimoto's
thyroiditis)

Presentation of a Case (Myxoedema): Case No. 2

- The face is puffy with periorbital swelling and baggy eyelids, the patient looks apathetic.
- Outer 1/3rd of the eyebrow is absent or reduced.

My diagnosis is **Myxoedema**.

Q: What else do you like to see?

A: I want to talk to the patient (to see the voice). Also, I want to see the leg for non-pitting oedema, ankle jerk. Also I want to examine the thyroid gland, eyes, skin.

Presentation of a Case (Myxoedema): Case No. 3

- Present as in case no. 2 plus thyroid gland is diffusely enlarged and there is bilateral exophthalmos.

My diagnosis is **Graves' disease with hypothyroidism**.

Q: What **else** do you like to see?

A: I want to see for pretibial myxoedema.

Presentation of a Case (Myxoedema): Case No. 4

- Present as in case no. 3, **plus** firm or rubbery, non-tender, no bruit and no exophthalmos.

My diagnosis is **Myxoedema** due to Hashimoto's thyroiditis.

N.B.: For details of each disease see later in this chapter.

THYROTOXICOSIS (HYPERTHYROIDISM)

Instruction by the examiner:

- Examine the thyroid gland and relevants. Or, show me the thyroid status.

Presentation of a Case:

- Thyroid gland is diffusely enlarged (or nodular or multinodular), 7×6 cm, non-tender, firm in consistency, freely mobile, no retrosternal extension, no palpable lymph node. Bruit is present.
- The patient has tremor of outstretched hands.
- Palms of the hands are warm and sweaty.
- Pulse: 120/min (Tachycardia. Pulse may be normal, if the patient is on β -blocker).

My diagnosis is **Diffuse goitre with thyrotoxicosis**.

N.B. There may be atrial fibrillation, ectopics and high volume pulse in thyrotoxicosis.



Toxic multinodular goitre



Cachexia in thyrotoxicosis



Apathetic thyrotoxicosis

Q: What else do you want to examine?

A: I want to examine the eye, cardiovascular system and jerks.

Q: What do you think the cause of thyrotoxicosis in this case?

A: As follows (mention the causes of that case by looking at face and neck):

- In young patient with diffuse goitre and exophthalmos, the likely cause is Graves disease (even if no exophthalmos, still it can be *Graves* disease).
- In the middle-aged with nodular goitre (single or multiple), the likely cause is toxic nodular or toxic multinodular goitre.

Causes of thyrotoxicosis:

1. Graves' disease: commonest cause (76%).
2. Toxic multinodular goitre (14%).
3. Toxic nodular goitre (5%, toxic adenoma or hot nodule called Plummer's disease).
4. Thyroiditis (subacute thyroiditis, also called De Quervain's thyroiditis and post-partum thyroiditis. All are transient).
5. Hashimoto's thyroiditis (initially, but later hypothyroidism develops).
6. Factitious thyrotoxicosis (self intake of thyroxine).
7. Iodine induced (*Jod-Basedow's phenomenon*) and drug (amiodarone).
8. Others (rare):
 - Carcinoma of thyroid (follicular).
 - Struma ovarii (secretes thyroid hormone).
 - Hydatidiform mole and choriocarcinoma (both secrete thyroid-stimulating hormone).

Q: Ask few **questions**, or what **history** do you like to take in thyrotoxicosis?

A: Ask the patient:

- Do you prefer hot or cold? (Heat intolerance).
- Do you have excessive sweating? (Sweating is excessive).
- Are you losing weight? (Weight loss is common).
- How is your appetite? (appetite is increased).
- How is your bowel habit? (Diarrhoea may occur).
- In females, ask about menstruation (Usually amenorrhoea in thyrotoxicosis).
- Others: palpitation, tremor, irritability, insomnia, anxiousness or nervousness.

N.B. If any patient complains of loss of weight despite good appetite, the likely diagnosis is thyrotoxicosis (other cause may be diabetes mellitus. However, loss of appetite in thyrotoxicosis may occur in the elderly).

Q: What **investigations** do you suggest in thyrotoxicosis?

A: As follows:

1. Thyroid function tests:

- Radioactive iodine uptake test (RAIU). RAIU shows rapid uptake and rapid turnover (there is high uptake in 2 or 4 and 24 hours and rapid fall after 48 hours).
- Thyroid scanning (technetium scintigraphy is better than RAIU test because it is quicker to perform and requires lower dose of radioactivity).
- Ultrasonography of the neck (to see single, multinodular or diffuse goitre).
- FT₃, FT₄ and TSH (low TSH, high T₃ and T₄. But in T₃ toxicosis, T₃ is high but TSH and T₄ is normal or near normal).

2. To find out causes:

- Thyroid auto-antibody: For Graves disease—TSH receptor stimulating antibody.
- Also, antiperoxidase and antithyroglobulin antibody (very high in Hashimoto's thyroiditis, but slight to moderate high in Graves disease).

3. Other tests:

- ECG.
- Chest X-ray (to see retro-sternal extension of goitre and cardiomegaly).
- Blood sugar (secondary DM may occur).
- Serum cholesterol (low in thyrotoxicosis).
- FNAC (if goitre is present).
- For ophthalmopathy (in Graves disease, see page 511).

Q: What are the causes of thyrotoxicosis with low radioiodine uptake?

A: Causes of thyrotoxicosis with low radioiodine uptake:

- Subacute thyroiditis (De Quervain's thyroiditis).
- Postpartum thyroiditis.
- Factitious thyrotoxicosis.
- Iodine induced (patient on iodine or amiodarone, which contains iodine).
- Ectopic thyroid tissue producing thyrotoxicosis (struma ovarii, choriocarcinoma and hydatidiform mole).

Q: How to treat thyrotoxicosis?

A: 3 modes of treatment: Drugs (carbimazole and propylthiouracil), radioiodine therapy and surgery.

Drug therapy:

1. Carbimazole or propylthiouracil: reduce the synthesis of thyroid hormones by inhibiting the iodination of tyrosine.
 - Carbimazole 40 to 60 mg daily. When the patient is euthyroid, reduce the dose, then 5 to 20 mg daily for 18 to 24 months. Periodic CBC should be done (may be agranulocytosis). Also, FT4 and TSH should be measured.
 - Propylthiouracil 100 to 200 mg 8 hourly. Dose is reduced when the patient is euthyroid.
2. β -Blocker: Propranolol (up to 160 mg/day). It reduces sympathetic symptoms (such as tremor, tachycardia and sweating).

Indications of drug:

- Usually given in first episode in patient <40 years of age.
- Small goitre.
- Mild features of thyrotoxicosis.

Disadvantages of drugs:

- Relapse in 50% cases within 2 years of stopping the drug (surgery or radioiodine or long term drug therapy may be needed in such case).
- Compliance may be poor.
- Costly.

Complication of drugs:

- Carbimazole can cause hypersensitive skin rash and agranulocytosis (0.1%). Other side effects are nausea, vomiting, arthralgia, jaundice (May be started in low dose to see skin rash. If no rash, then gradually increase the dose up to the standard level).

- PTU can cause skin rash, nausea, vomiting, agranulocytosis, hepatotoxicity. It has small but definite risk of hepatotoxicity, may result in liver failure requiring liver transplantation and even death. So, it should be considered second line therapy, only to be used during pregnancy or breastfeeding, or if side effects of carbimazole.

N.B.: If patient on carbimazole therapy develops sore throat or fever, which may be due to agranulocytosis, drug should be stopped and his/her doctor should be informed.

Radioiodine therapy:

It acts by destroying the functioning thyroid cells and inhibiting their ability to replicate. Depending on the size of goitre, 5 to 10 mCi is given orally. It is effective in 75% cases in 4 to 12 weeks. In this period, propranolol is given. In severe cases, carbimazole may be given, which should be started 48 h after radioiodine therapy. If the drug is started before 48 h, it reduces the efficacy of radioiodine.

Indications of radioiodine therapy:

- Usually, above 40 years of age (however, may be used in young).
- Recurrence after surgery or drugs, irrespective of age.
- Toxic multinodular goitre or toxic adenoma or hot nodule.
- In early age, with other major serious illness.
- Some cases of carcinoma thyroid (follicular, papillary after surgery).
- Ablative therapy with severe atrial fibrillation, also in heart failure.
- Psychosis.
- Poor drug compliance.
- Hypersensitivity to the drug.

Contraindications of radioiodine therapy:

- Pregnancy or planned pregnancy within 6 months of treatment.
- During lactation.
- Active or malignant Graves ophthalmopathy.

Disadvantages of radioiodine therapy:

- Hypothyroidism: It occurs in 40% in first year and 80% in 15 years.
- Early discomfort and exaggeration of hyperthyroidism may occur due to radiation thyroiditis (so, antithyroid drug should be given to make the patient euthyroid, which should be stopped 2 to 5 days before radioiodine therapy).
- Exacerbation of ophthalmopathy.

N.B.: Remember the following points:

- *In severe thyrotoxicosis, initially carbimazole is given for 4 to 8 weeks. Then radioiodine therapy is given. Carbimazole is stopped 48 hours before radioiodine therapy. If no response after 12 to 24 weeks, a second dose of radioiodine is given.*
- *In women of reproductive age, pregnancy must be excluded before administration of ^{131}I and avoided for 6 months thereafter.*
- *Men are also advised against fathering children for 6 months after receiving ^{131}I .*

Surgery (usually subtotal or near total thyroidectomy):

Antithyroid drug should be given to make the patient euthyroid before surgery. Potassium iodide should be added 60 mg 8 hourly, 2 weeks before operation. It inhibits thyroid hormone release, reduces the size and vascularity of gland, making surgery easier.

Indications of surgery:

- Large goitre or multinodular goitre.
- Relapse or no response to drug.
- Drug hypersensitivity.
- Non-compliance with drug.
- Suspicion of malignancy.
- Pressure effect.
- Cosmetic purpose.

Complications of surgery:

- Hypothyroidism in 25%.
- Transient hypocalcaemia (10%).
- Permanent hypoparathyroidism (1%).
- Recurrent laryngeal nerve palsy causing hoarseness of voice due to vocal cord palsy (1%).

N.B. In toxic nodular or multinodular goitre, treatment of choice is radioiodine therapy or surgery. Drug treatment is not helpful.

Q: What is thyrotoxic periodic paralysis (TPP)?

A: If a thyrotoxic patient develops sudden or periodic weakness, it is called TPP. It is due to hypokalaemia (caused by entry of potassium into the cell), common in Asians. It may occur following excess of carbohydrate or glucose or heavy exercise and persists for 7 to 72 hours. Treatment of thyrotoxicosis improves the condition.

Q: How to treat thyrotoxicosis with atrial fibrillation?

A: AF occurs in 10% cases, common in elderly >60 years, more in toxic multinodular goitre, may occur in subclinical hyperthyroidism. It is treated in the following ways:

- β -Blocker: Propranolol (digoxin has little role). Verapamil and amiodarone may be used, if β -blocker is contraindicated.
- Antithyroid drug, followed by radioiodine therapy.
- Anticoagulant: Aspirin in elderly and warfarin in younger.
- 50% AF reverts spontaneously to sinus rhythm.
- If no response and AF is persistent: cardioversion may be done, provided T_4 and TSH are normal.

Q: What is thyrotoxic crisis? How to treat?

A: It is characterized by life threatening increase in signs and symptoms of thyrotoxicosis (also called thyroid storm).

Features of thyrotoxic crisis are:

- High fever.
- Restlessness, agitation and irritability.
- Nausea, vomiting, diarrhoea and abdominal pain.
- Tachycardia, AF and cardiac failure in elderly.
- Confusion, delirium and coma.

Precipitating factors for thyrotoxic crisis:

- Infection.
- Stress.
- Surgery in unprepared patient.
- Following radioiodine therapy (due to radiation thyroiditis).

Diagnosis:

Mostly clinical and high degree of suspicion is vital. FT₃, FT₄ and TSH should be done immediately.

Treatment (before starting treatment, blood sample is taken for T₃, T₄ and TSH):

- The patient should be treated in ICU.
- Propranolol 80 mg 6 hourly (or 1 to 5 mg IV 6 hourly).
- IV fluid (normal saline and glucose).
- Carbimazole 40 to 60 mg daily. Or propylthiouracil 150 mg 6 hourly (if needed, through Ryle's tube). Carbimazole can be given per-rectally also.
- Other therapy: Sodium ipodate (a radiographical contrast media), 500 mg daily is rapidly effective. Or potassium iodide or Lugol's iodine may be given. Dexamethasone 2 mg 6 hourly and amiodarone are also effective.
- Broad spectrum antibiotic.
- General measures: Control of temperature and O₂ therapy.
- After 10 to 14 days, the patient can usually be maintained on carbimazole alone.

Mortality rate in thyrotoxic crisis is 10%.

Q: What is factitious thyrotoxicosis?

A: Deliberate intake of thyroxine to reduce weight, usually in emotionally disturbed person. Clues for diagnosis are high thyroid hormones and low radioiodine uptake. Thyroglobulin level is zero or low, high ratio of T₄:T₃ = 70:1 (in conventional thyrotoxicosis, the ratio is 30:1). Combination of negligible radioiodine uptake, high T₄:T₃ ratio and low thyroglobulin is diagnostic.

Q: What is apathetic hyperthyroidism?

A: It occurs in elderly in which, there is lack of features of hyperthyroidism. Only features may be unexplained weight loss or cardiac features such as atrial fibrillation, tachycardia or heart failure, which masks thyrotoxicosis. High degree of suspicion is essential for diagnosis.

N.B. Children may present with excess growth, behaviour problem like hyperactivity and increase in weight rather than loss.

THYROID DISORDERS IN PREGNANCY

- Mild goitre may be present normally. No treatment is necessary.
- Thyrotoxicosis (Graves' disease, toxic nodular or multinodular).
- Hypothyroidism.

THYROTOXICOSIS IN PREGNANCY

Like hypothyroidism, it is not a common disease in pregnancy but may occur in 2:1000. In most of the cases, hyperthyroidism may be present before pregnancy (either known or subclinical).

Causes of thyrotoxicosis: As above. Graves' disease is the commonest cause of thyrotoxicosis in pregnancy.

Complications: Poorly controlled maternal thyrotoxicosis can cause—

- Foetal loss e.g., Still birth.
- Intrauterine growth retardation.
- Prematurity.
- Congenital anomalies.
- Abortion.
- Cardiac abnormalities (arrhythmia, foetal tachycardia).

Diagnosis of thyrotoxicosis in pregnancy may be difficult, because most of the features of pregnancy may simulate features of thyrotoxicosis. High degree of suspicion is essential for the diagnosis. Common features are—

- Tachycardia
- Tremor
- Excitability
- Excessive sweating,
- Heat intolerance,
- Frequent loose motion.

Clues for the diagnosis are:

- Previous H/O thyroid disease.
- Inability to gain weight in pregnancy.
- Relatively more tachycardia than expected.
- Thyroid gland—more enlarged, firm and presence of bruit.
- Exophthalmos and/or eye signs.

Investigations:

- High FT₄, FT₃ and low TSH level is suggestive of thyrotoxicosis (because of high thyroxine binding globulin, total T₄ and T₃ are high and TSH is low, this test should not be done).
- USG of neck.
- Thyroid autoantibody may be done.

N.B. Radioactive iodine uptake test should never be done during pregnancy.

Treatment: Very vital. Aims to control of maternal thyrotoxicosis and not to interfere with normal foetal thyroid development.

- Mostly treated by antithyroid drugs. In some cases, surgery may be necessary.
- Drugs: Propylthiouracil, Carbimazole.
- Propylthiouracil is preferred in 1st trimester, 100 to 150 mg, 8 hourly. Carbimazole can cause foetal goitre and scalp skin defect in child called aplasia cutis.
- PTU should be replaced by carbimazole from the beginning of 2nd trimester, because of its potential hepatotoxicity.
- However, if PTU is not available, carbimazole (<15 mg/day) should be given.
- Both drugs can cross placenta, so given in lowest dose, <150 mg for PTU or <15 mg of carbimazole daily to prevent foetal hypothyroidism and goitre.
- Drug should be reduced near term. TRAb is measured in last trimester. If not high, the drug can be stopped 4 weeks before delivery (to prevent neonatal goitre and hypothyroidism).
- After delivery, chance of relapse is high. Propylthiouracil can be given after delivery and breast-feeding should be continued, as little is excreted in breast milk.
- If carbimazole is to be continued, breast feeding should be stopped.
- Surgery may be necessary in some cases, such as if control is not possible with drugs or hypersensitivity to drug or if the patient's compliance is poor. It should be done during 2nd trimester.
- Beta blocker (Propranolol) may be given along with anti-thyroid drug for symptomatic relief.

N.B. Radioiodine therapy is absolutely contraindicated in pregnancy.

BRIEF NOTES ON POST-PARTUM THYROIDITIS

- May occur in 5 to 10% cases within first 6 months of delivery.
- Cause is unknown. Mostly autoimmune, which remains suppressed during pregnancy but flares after delivery.
- Common in woman who have other autoimmune disease or family history of thyroid disease.
- Histology of thyroid shows thyroiditis with lymphocyte infiltration.
- Anti-peroxidase (antimicrosomal) antibody is found in early pregnancy. TSH receptor antibody is not present.
- Family history of thyroid disorder may be present.
- This may occur whenever biochemical abnormality of thyroid function is present in pregnancy (either hypothyroid, hyperthyroid or hyperthyroid followed by hypothyroid).
- Transient hyperthyroidism occurs due to release of thyroid hormone by anti-peroxidase antibody. Later hypothyroidism may occur. However, most cases remain euthyroid.
- 70% recur in subsequent pregnancy.

Diagnosis:

- History—Sign symptoms may not be significantly present. High degree of suspicion is essential.
- FT₃, FT₄ are increased, TSH is decreased.
- Radioactive Iodine uptake—decreased (this test should be avoided if breast feeding).

Treatment:

- Spontaneous recovery in 90% case in 3 to 6 months.
- Symptomatic: Propranolol may be given.
- Anti-thyroid drug is not necessary in most cases.
- Follow up is essential. Hypothyroidism is common in 50% case after 7 year.
- Radioiodine therapy is contraindicated.

Prognosis:

- Most cases recover spontaneously.
- Hypothyroidism may develop after some years.

BRIEF NOTES ON DE QUERVAIN'S THYROIDITIS

Def: de Quervain's thyroiditis is a virus induced transient inflammation of thyroid gland. It is caused by Coxsackie B4, also may be associated with influenza, infectious mononucleosis, measles, mumps, adenovirus. It can be precipitated by drugs such as interferon- α , lithium.

Clinical features: It is more in female, 20 to 40 years.

- Patient usually presents with pain over thyroid or neck, which radiates to jaw, ear and which is worsened by coughing, swallowing or movement of neck.
- Other features are fever, dry cough, throat pain, headache, body ache, palpitation and intolerance to heat.
- Features of thyrotoxicosis such as fine tremor of outstretched hands, warm and sweaty palms, tachycardia are present.
- Thyroid gland is enlarged and tender, regional lymphadenopathy may be present.
- Hyperthyroidism followed by transient hypothyroidism may occur.

Investigations:

- CBC and ESR (ESR is typically high).
- FT_3 , FT_4 are high, TSH is low. This may persist for 4 to 6 weeks.
- Radioactive Iodine uptake is low.
- FNAC shows presence of giant cells.
- Transient rise of thyroid auto-antibodies in low titre in the serum may be found.

Treatment: It is usually self-limiting.

- Symptomatic: NSAID.
- Propranolol may be used.
- If no response: Prednisolone 40 mg/day for 3 to 4 weeks may be needed.
- Antithyroid drug should not be given.
- Thyroxine may be given temporarily, if hypothyroidism. Long term thyroxine is not necessary.

Prognosis: Complete recovery usually occurs in 4 to 6 months.

HYPOTHYROIDISM

Instruction by the examiner:

- Look at the face. What are your findings? What else do you want to examine?
- Examine the leg. What are your findings? What else do you want to examine?
- Examine the thyroid gland and the relevants.

Proceed as follows:

- **Instruction 1:** Mention the findings of the face (see below). Then mention, 'I want to examine the legs (non-pitting oedema and slow relaxation of ankle jerk) and skin. Also, I want to talk with the patient (hoarse and croaky voice) and examine the thyroid gland'.
- **Instruction 2:** Mention the findings in legs. Then mention, 'I want to examine the face, talk with the patient and examine the skin and thyroid gland'.
- **Instruction 3:** Examine the thyroid gland systematically. Then mention, 'I want to examine the face, talk with the patient and examine legs and skin'.



Myxoedema



Nonpitting oedema in myxoedema



Goitrous hypothyroidism



Graves disease (hypothyroid)

Presentation of a Case (Only Myxoedema, No Goitre): Case No. 1

- The face is puffy with periorbital swelling, baggy eyelids and malar flush. There is also loss of outer 1/3rd of eyebrows.
- Skin: Dry, rough, cold and thick (there may be yellow skin due to carotinaemia, vitiligo and erythema ab igne).
- Non-pitting oedema in leg and generalized swelling of whole body.
- Voice: Low pitched, slurred, hoarse and croaky (hypothyroidism is diagnosed by talking over telephone).
- Ankle jerk (slow relaxation).
- Pulse: 50/min (bradycardia).
- Thyroid gland (not enlarged).

My diagnosis is **Myxoedema (non-goitrous)**.

Q: Ask some **questions** to the patient. Or, what **history** would you like to take?

A: When the patient answers, hear the voice and comment on it.

- Do you prefer hot or cold? (Cold intolerance).
- Are you gaining weight? (Increased weight gain).
- Tell me about your bowel habit (Usually constipation).
- In females: Ask about menstruation (Usually menorrhagia).

(Other history: Drug, thyroid surgery and radioiodine therapy to find out causes).

Q: What do you think of the **cause** in this case (**non-goitrous** hypothyroidism)?

A: More likely **Autoimmune** or **spontaneous atrophic hypothyroidism** (common cause). Other causes are:

- Following radioiodine therapy.
- After surgery (total thyroidectomy, check for any scar mark in neck).
- Thyroid aplasia (rare).
- TSH deficiency (rare, secondary hypothyroidism).

Presentation of a Case (Myxoedema with Goitre): Case No. 2

- Non-pitting oedema in leg and generalized swelling of whole body plus above findings in case no 1.
- **Plus if** there is goitre, mention it (or if no goitre, tell non-goitrous).

My diagnosis is **Myxoedema (goitrous or non-goitrous, mention according to your findings)**.

Presentation of a Case (Myxoedema with Goitre): Case No. 3

- There is goitre (mention single or multinodular), non-tender, firm in consistency, freely movable and no bruit.
- Or, thyroid gland is diffusely enlarged, non-tender, firm and rubbery, freely movable and no bruit.
- Plus above findings in face, legs, skin, also mention voice as in case no 1.

My diagnosis is **Myxoedema with goitre (diffuse or nodular, mention accordingly)**.

Q: What do you think of the **causes** of diffuse **goitrous hypothyroidism**?

A: Hashimoto's thyroiditis (if bilateral exophthalmos with diffuse goitre, mention Graves' disease with hypothyroidism).

Q: What are the **other causes** of hypothyroidism in this case (goitrous hypothyroid)?

A: Other possibilities are:

- Drugs: Lithium, amiodarone and iodide.
- Endemic iodine deficiency (less common).
- Rarely, dyshormonogenesis and infiltrative disease (amyloidosis, sarcoidosis).

Presentation of a Case (Myxoedema with Graves Disease): Case No. 4

- There is diffuse goitre plus mention the findings in as in case no 1.
- **Plus** there is bilateral exophthalmos and pretibial myxoedema.

My diagnosis is **Graves disease with hypothyroidism** (for details see Graves disease).

Q: Why hypothyroidism in Graves disease?

A: Natural history of Graves disease is hyperthyroidism, followed by euthyroidism and hypothyroidism (this may occur following radioiodine therapy or after surgical treatment).

Q: What investigations should be done to diagnose myxoedema or hypothyroidism?

A: As follows:

1. Serum FT₃, FT₄ and TSH (both T₃ and T₄ are low, TSH is high).
2. Autoantibody (for Hashimoto's thyroiditis): Antiperoxidase and antithyroglobulin (both are very high).
3. Other tests (not for diagnosis, but to check other effects):
 - ECG (low voltage tracing, sinus bradycardia and T wave inversion).
 - USG of neck (to see any goitre).
 - Chest X-ray (cardiomegaly due to pericardial effusion or heart failure).
 - Serum lipid profile: cholesterol and triglyceride (high).
 - CPK, LDH and SGOT (all may be high, these are not done routinely).

Q: What single investigation should be done in myxoedema?

A: Single test is TSH (and other one is T₄. But T₃ may be normal, as it is converted from T₄).

Q: What are the thyroid functions in secondary hypothyroidism?

A: Low FT₃, FT₄ and TSH (usually all thyroid hormones are low).

Q: If a patient has low T₃, T₄ and TSH, what are the causes? How to investigate in such case?

A: Causes may be in the pituitary or hypothalamus. TRH stimulation test should be done.

- After giving TRH, if TSH is high: the cause is in the hypothalamus.
- If there is no or little rise of TSH: the cause is in the pituitary.

Q: What is the treatment of hypothyroidism?

A: Thyroxine: It should be started with low dose. The dose should be increased gradually after 3 weeks. Single dose is preferable and should be taken before breakfast (recently, according to some study, thyroxine is better absorbed if taken at night. Vitamin C may help for absorption). TSH should be repeated after 6 to 8 weeks. If TSH is normal, maintenance dose should be continued as a single daily dose. For follow up, annual thyroid function test should be done (TSH should be within normal range and FT₄ should be upper limit of normal).

***N.B.:** If the patient has deficiency of cortisol (as in hypopituitarism or Addison's disease), corticosteroid should be given first and then thyroxine. Otherwise, if thyroxine is given first without correcting cortisol deficiency, there will be severe Addisonian crisis.*

Q: Why thyroxine should be started in low dose?

A: Because if high dose is given, it may precipitate anginal attack.

Q: How long will you continue thyroxine?

A: Lifelong.

READ THE FOLLOWING TOPICS IN RELATION TO HYPOTHYROIDISM

Q: What is hypothyroidism?

A: It is a clinical condition due to deficiency of thyroid hormone.

Q: What are the causes of hypothyroidism?

A: As follows:

1. Autoimmune or spontaneous atrophic hypothyroidism (commonest);
2. Hashimoto's thyroiditis.
3. Graves disease (associated with TSH receptor blocking antibody).
4. Radioiodine therapy for thyrotoxicosis.
5. After surgery (thyroidectomy).
6. Post-radiotherapy in neck.
7. Drugs: Lithium, amiodarone and antithyroid drug therapy.
8. Others:
 - Endemic iodine deficiency.
 - Post-partum thyroiditis.
 - Rarely, dyshormonogenesis.
 - Secondary to hypopituitarism and hypothalamic disorders (rare).

Q: What are the causes of **goitrous** hypothyroidism?

A: As follows:

- Hashimoto's thyroiditis.
- Graves' disease (in such case, there is also exophthalmos and diffuse goitre with dermopathy).
- Endemic iodine deficiency (less common).
- Drugs: Lithium, amiodarone, iodide.
- Rarely, dyshormonogenesis.

Q: What are the causes of **non-goitrous** hypothyroidism?

A: As follows:

- Autoimmune or idiopathic (spontaneous atrophic)—commonest cause.
- Following radio-iodine therapy for thyrotoxicosis.
- Post-radiotherapy in the neck.
- After surgery (thyroidectomy).
- Secondary to hypopituitarism, hypothalamic disorders (rare).

Q: What are the causes of **transient** hypothyroidism? **How to treat?**

A: Causes are:

- Subacute thyroiditis.
- Post-partum thyroiditis.
- Drug induced.

Treatment: thyroxine should be given temporarily. Follow up measurement of TSH should be done.

Q: How to treat an elderly patient with hypothyroidism?

A: Treatment is same. But care should be taken in patient, who is suffering from ischaemic heart disease. After thyroxine therapy, it may precipitate angina and myocardial infarction (so, it should be started in low dose).

Q: What bedside test will you do in myxoedema?

A: Ankle jerk. There is slow relaxation called **hung up reflex** (other jerks may show slow relaxation).

Q: How slow relaxation is best elicited in the ankle? Why slow relaxation?

A: By kneel-down position on a chair or bedside. Slow relaxation is due to decreased muscle metabolism.

Q: Why non-pitting oedema?

A: Due to deposition of mucopolysaccharide substances, hyaluronic acid and chondroitin sulphate. These are also responsible for hoarse voice, carpal tunnel syndrome and body swelling.

Q: What is the difference between myxoedema and hypothyroidism?

A: Myxoedema is severe form of hypothyroidism due to deposition of mucopolysaccharide substances, but all hypothyroidism may not be myxoedematous.

Q: What are the types of anaemia in hypothyroidism?

A: Anaemia may be:

- Normocytic normochromic (common).
- Iron deficiency, if menorrhagia (in female).
- May be macrocytic due to associated pernicious anaemia.

Q: What are the causes of anaemia in hypothyroidism?

A: Causes of anaemia:

- Anaemia of chronic disorder.
- Iron deficiency.
- Vitamin B12 deficiency.
- Folate deficiency.
- Other factors responsible: Menorrhagia in female, anorexia.

N.B. Macrocytosis in peripheral blood, but normoblastic bone marrow occurs in hypothyroidism.

Q: What is the difference between primary and secondary hypothyroidism?

A: As follows:

- Primary hypothyroidism involves thyroid gland associated with myxoedema.
- Secondary hypothyroidism is due to the involvement of pituitary or hypothalamus. In such cases, myxoedema is rare, there are other features of hypopituitarism.

Q: What is subclinical hypothyroidism (borderline hypothyroidism or compensated euthyroidism)? How to treat?

A: In this condition, T_3 and T_4 are in the lower limit of normal but TSH is slightly high. The patient may be clinically euthyroid. This may persist for many years, though overt hypothyroidism may occur. Conversion to overt hypothyroidism is more common in men or when thyroid peroxidase (TPO) antibody is present or when TSH level is more than 10 mU/L.

Treatment:

- Thyroxine therapy may be given if TSH is persistently raised above 10 mU/L or when there are symptoms or high titre of thyroid antibodies or lipid abnormalities.
- If only TSH is marginally high with vague symptoms, thyroxine may be given sometimes.
- However, in female TSH should be normalized during pregnancy to avoid any adverse effect on foetus.
- If TSH is marginally raised, the test should be repeated after 3 to 6 months.

Q: What are the cardiovascular complications in myxoedema?**A:** As follows:

- Sinus bradycardia.
- Pericardial effusion.
- Congestive cardiac failure.
- Ischaemic heart disease.
- Hypertension.
- Atherosclerosis (because of hypercholesterolaemia).

Q: What are the neurological features in hypothyroidism?**A:** As follows:

- Carpal tunnel syndrome (or tarsal tunnel syndrome).
- Slow relaxation of ankle jerk.
- Psychosis (myxoedema madness).
- Myxoedema coma.
- Cerebellar syndrome.
- Deafness (Trotter's syndrome).
- Epileptic fit (due to SIADH).
- Proximal myopathy.
- Others: Peripheral neuropathy, myotonia (Hoffman's syndrome), pseudodementia, drop attack.

Q: What is Hoffman's syndrome?**A:** In myxoedema, there may be myotonia with pain and swelling in the muscles after exercise called Hoffman's syndrome.**Q: What is Pendred syndrome?****A:** It is an inherited disorder (autosomal recessive) associated with sensorineural deafness and goitre. It is due to the inborn error of thyroid hormone synthesis.**Q: What is sick euthyroid syndrome?****A:** In any severe acute non-thyroidal illness or after surgery, there may be abnormal thyroid function tests, although the patient is euthyroid. It is called sick euthyroid syndrome. It may occur after myocardial infarction, pneumonia, cerebrovascular disease and drugs (dopamine and steroids). Usually, there is low TSH, high T_4 and normal or low T_3 . Levels are usually mildly below normal and are thought to be mediated by interleukins (IL-1 and IL-6). Test should be repeated after recovery of systemic illness. Biochemical thyroid function should not be done in patients with acute non-thyroidal illness, unless there is good evidence of thyroid disease (such as goitre and exophthalmos).

Mechanisms of sick euthyroid syndrome:

- Reduced production or affinity of TBG to T_4 and T_3 .
- Reduced peripheral conversion of T_4 to T_3 , occasionally, more rT_3 (inactive reverse T_3).
- Reduced hypothalamic pituitary TSH production; hence low T_3 and T_4 .

Q: What is myxoedema coma?

A: Myxoedema coma is characterized by depressed level of consciousness or even coma. Convulsion may occur. It is rare, may occur in severe hypothyroidism, usually in elderly. CSF studies show high pressure and high protein content. 50% mortality.

Q: What are the causes or factors that precipitate myxoedema coma?

A: As follows:

- Syndrome of inappropriate ADH secretion (SIADH). Coma is due to hyponatraemia.
- Hypoxaemia.
- Hypercapnia.
- Hypothermia.
- Hypoglycaemia.
- Other factors: Cardiac failure, infection, use of sedative.

Q: How to treat?

A: Should be treated in ICU. Before starting treatment, blood is taken for FT_3 , FT_4 , TSH and cortisol.

1. T_3 (rapidly acting) 20 μg m, 8 hourly usually IV given (parenteral T_4 is not available, also slow to start action). If parenteral T_3 is not available, oral thyroxine (through Ryle's tube, if the patient is unconscious).
2. IV hydrocortisone: 100 mg 8 hourly (especially if suspicion of hypopituitarism).
3. Other treatment:
 - Slow rewarming.
 - High flow O_2 therapy.
 - IV fluid and glucose.
 - Antibiotic.
 - Assisted ventilation may be necessary (as in any unconscious patient).

Q: What is myxoedema madness?

A: It may occur in severe hypothyroidism in elderly. There is dementia or psychosis or delusion. Sometimes, these features may occur shortly after starting thyroxine replacement. Depression is common in hypothyroidism.

Q: If the patient has ischaemic heart disease with hypothyroidism, how to treat?

A: As follows:

- Thyroxine should be given in low dose (25 μg m). Dose should be increased slowly up to the optimum dose.
- β -Blocker (propranolol) should be added.
- Coronary dilator, calcium antagonist may be added.
- If no improvement or angina is worsen, coronary angiography followed by angioplasty or stenting or coronary artery bypass surgery may be done.

Q: What are the autoimmune diseases associated with thyroid disorder?

A: Pernicious anaemia, Addison's disease, Sjögren's syndrome, DM, autoimmune haemolytic anaemia, SLE, autoimmune hepatitis, primary biliary cirrhosis, premature ovarian failure.

HYPOTHYROIDISM IN PREGNANCY

- It is rare during pregnancy (0.5 to 3% case).
- Infertility is common in hypothyroidism.
- If hypothyroidism occurs, probably it was present before pregnancy (either known case or subclinical).
- Sometimes may be difficult to diagnose as most of the symptoms of pregnancy may simulate hypothyroidism.
- High degree of suspicion is vital for the diagnosis.
- If there is suspicion of hypothyroidism, diagnosis is confirmed by clinical findings and thyroid function tests.

Complications of pregnancy with hypothyroidism:

- Prematurity.
- Pre-eclampsia.
- Abortion.
- Still birth.
- Abruptio placenta.
- Cardiac arrhythmia.
- Congenital anomaly.
- Postpartum haemorrhage.

Causes of hypothyroidism: Autoimmune (spontaneous atrophic hypothyroidism and Hashimoto's thyroiditis) are commonest cause. Other causes are same as in other hypothyroidism.

Investigation: FT_3 and FT_4 are low, TSH is high (avoid performing total T_3 and T_4 . Radioactive iodine test is contraindicated).

Treatment:

- Thyroxine. Requirement of thyroxine is relatively high (40 to 50%) in pregnancy because of increased metabolism by the placenta and also increased serum TBG in pregnancy, which binds thyroxine, resulting in less FT_3 and FT_4 .
- Dose should be adjusted according to FT_4 and TSH levels (TSH should be at the lower limit of normal and FT_4 should be at the upper limit of normal).
- T_4 usually does not cross placenta.
- After delivery, breastfeeding should be continued.
- FT_4 and TSH should be measured in each trimester.

N.B. Thyroxine is less absorbed if calcium and iron are given together. So it should be given 4 hours before calcium and iron therapy.

Q: What is Hashimoto's thyroiditis?

A: It is an autoimmune thyroiditis characterized by destructive lymphoid infiltration of thyroid leading to atrophic change with regeneration, fibrosis and goitre formation. It is more common in middle aged woman.

- Goitre is usually diffuse, moderately enlarged, firm or rubbery in consistency. Sometimes, soft to hard.
- Antithyroid antibody (very high, >1000 IU/L): Antimicrosomal (anti TPO) in 90% and antithyroglobulin antibodies (no rise of TSH receptor antibody).
- About 25% patients are hypothyroid at presentation. In the remaining patients, serum T₄ is normal and TSH is normal or raised. Hypothyroidism develops later. Initially, the patient may present with features of toxicosis called Hashitoxicosis.
- In young patients (<20 years), ANF may be positive.
- It is an autoimmune disease; so, it may be associated with other autoimmune diseases like Addison's disease, DM, premature ovarian failure, rheumatoid arthritis, Sjögren's syndrome, ulcerative colitis, autoimmune haemolytic anaemia.
- Treatment: Thyroxine should be given (even if the patient is not hypothyroid, it reduces the size of goitre also). TSH should be at the lower normal limit.

N.B.: Rarely, there is increased risk of developing thyroid lymphoma.

Q: What is the radioiodine uptake in Hashimoto's thyroiditis?

A: It shows the following:

- Initially: Increased (toxic phase).
- After few days or weeks: Normal uptake.
- Later on: Less uptake (hypothyroid phase).

Q: What are the histological findings in Hashimoto's thyroiditis?

A: As follows:

- Lymphocyte infiltration, also monocyte and plasma cell.
- Hyperplasia and fibrosis.
- Hurthle cell.

BRIEF NOTES ON CRETINISM

Q: What is cretinism?

A: It is defined as hypothyroidism due to congenital deficiency of thyroid hormone, also called congenital myxoedema. Features are as follows:

Features in neonates:

- Prolonged physiological jaundice.
- Hoarse cry.
- Lethargy, somnolence, excessive sleepy.
- Constipation.
- Feeding problem.
- Delayed passage of meconium.
- Hypotonia.
- Typical facies (protruded tongue, puffy eyelids, wrinkled foreheads) may be present

Features in older babies:

- Characteristic facies: Dull and so called idiotic look, large head, sparse hair, broad flat nose with big nostrils, widely set eyes (hypertelorism), thick everted lips with macroglossia.
- Pot belly with umbilical hernia.
- Skin is dry, scaly, rough, cold and pale yellow (carotenaemia). Hair is sparse, coarse and brittle.
- Delayed developmental milestones such as delayed dentition, delayed crawling etc.
- Hoarse voice.
- Short stature.
- Thick and short neck with presence of supraclavicular pad of fat.
- Lethargy and hypotonia.
- Mental retardation.

In older children: typical features of hypothyroidism are present.



Typical facies in cretinism



Pot belly and umbilical hernia in cretinism



Juvenile hypothyroidism



Hypothyroidism in early childhood

Diagnosis: In the early age, high degree of suspicion is essential for the diagnosis. Routine screening of neonates using a filter paper spot technique by heel-prick for TSH is done for diagnosis.

Treatment:

- Thyroxine should be started immediately.
- If treatment is delayed, permanent neurological and intellectual damage may occur.

Follow up: FT4 and TSH levels should be done as the following protocol—

- 0 to 6 months: every 6 weeks.
- 6 months to 6 years: every 3 months.
- >3 years: every 6 months.

GRAVES' DISEASE

Instruction by the examiner:

- Look at the patient. What are your findings? What else do you want to examine?
- Examine the thyroid gland.

(Remember, Graves disease may be hyperthyroid, euthyroid and hypothyroid.)

Presentation of a Case (Exophthalmos): Case No. 1

- There is unilateral or bilateral exophthalmos, periorbital oedema, chemosis, redness of eye, corneal ulceration, lid lag, lid retraction, ophthalmoplegia and diplopia (mention if present, in which direction and which eye).
- The face appears anxious, fidgety along with staring looks.
- Thyroid gland is diffusely enlarged, firm in consistency, non-tender and mobile.
- There is bruit (mention the site).
- Signs of thyrotoxicosis are present (tachycardia, tremor, warm and sweaty palm).

Diagnosis is **Thyrotoxicosis due to Graves disease**.

Q: Why it is Graves disease?

A: As there is exophthalmos and diffuse goitre.

Q: What else do you want to examine?

A: Dermopathy (pretibial myxoedema).

Q: What is the natural history of Graves disease?

A: It may be hyperthyroid, euthyroid, followed by hypothyroidism.

Presentation of a Case (Exophthalmos): Case No. 2

- There is unilateral or bilateral exophthalmos with no signs of thyrotoxicosis.

Diagnosis is **Euthyroid Graves disease**.



Graves disease (thyrotoxicosis)



Graves disease (euthyroid)



Graves disease (hypothyroid)

Presentation of a Case (Exophthalmos): Case No. 3

- There is unilateral or bilateral exophthalmos.
- Coarse, puffy facies, periorbital puffiness and baggy eyelids. Patient looks immobile and uninterested.
- Skin is dry, cold and scaly.
- Non-pitting oedema of leg and slow relaxation of ankle jerk.
- Voice is coarse and croaky.

Diagnosis is **Hypothyroid Graves disease**.

Q: What is Graves disease?

A: It is an autoimmune thyroid disease due to stimulating antibody to TSH receptors characterized by **triad** of:

- Exophthalmos.
- Diffuse goitre.
- Dermopathy (pretibial myxoedema).

Q: What is the cause of Graves disease?

A: Autoimmune disease due to IgG antibody against TSH receptor, producing excess thyroid hormones. TRAb acts similar to TSH. Common in female, M:F = 1:5. TRAb is of two types: (1) TSI, with 80 to 95% causing thyrotoxicosis and (2) TSH receptor-blocking antibody causing hypothyroidism.

Q: What is the significance of thyroid bruit? What is the cause of bruit?

A: It is pathognomonic of Graves disease and rarely occurs in other thyroid diseases. It indicates increased vascularity, probably due to an autoimmune mechanism.

Q: What is euthyroid Graves disease?

A: The patient is clinically and biochemically euthyroid, but there is ophthalmopathy.

Q: What investigations should be done in Graves disease?

A: As follows:

1. Thyroid function tests:

- Radioactive iodine uptake test (RAIU).
- Thyroid scanning.
- Ultrasonography of the neck (shows diffuse goitre).
- FT_3 , FT_4 and TSH.

2. Thyroid antibody:

- TSH receptor stimulating antibody (TRAb).
- Also, antiperoxidase and antithyroglobulin antibody (slightly high).

Q: How to treat Graves disease?

A: Graves disease is an autoimmune disease, which may present with hyper-, hypo- or euthyroid state.

- If thyrotoxicosis: medical, surgical or radioiodine therapy (discussed in thyrotoxicosis).
- If hypothyroidism: Thyroxine.
- If euthyroid: Treatment is only symptomatic and supportive.

Q: What is the **mechanism** of thyroid ophthalmopathy? What are the **changes** and how to **treat**?

A: It is immunologically mediated. Within the orbit, there is cytokine mediated proliferation of fibroblast, which secretes hydrophilic glycosaminoglycans. The following changes occur in ophthalmopathy:

- Excessive interstitial fluid with infiltration of chronic inflammatory cells in the orbit (such as lymphocytes, plasma cells and mast cells).
- Swelling and oedema of extraocular muscles.
- Increased retrobulbar pressure and eyeball is pushed forward (proptosis). In severe case, optic nerve compression may occur.

Clinical features: Increased lacrimation, gritty sensation in the eye, pain due to conjunctivitis or corneal ulcer, reduced visual acuity and diplopia. It increases with poor control of thyroid function and also following radio-iodine therapy. Ophthalmopathy is common in cigarette smokers. However, cigarette smoking is weakly associated with Graves disease.

Treatment:

- Reassurance and general treatment of eye. Methylcellulose eye drops (relieves grittiness).
- To prevent exposure keratitis—use sunglass, glass with special prism, lateral tarsorrhaphy (if corneal ulcer). Taping the eyelids and raising the head at night.
- Smoking must be stopped.
- In visual field defect, loss of visual acuity and papilloedema or progressive exophthalmos: steroid in high dose (prednisolone 60 to 120 mg/day) may be helpful. Pulse methylprednisolone may be used initially.
- In mild cases: oral selenium (100 µg twice daily for 6 months) improves quality of life, reduces ocular involvement and slows progression of disease.
- Immunosuppressants agents such as ciclosporin may be given with prednisolone.
- In severe cases: irradiation of the orbit.
- If no response in 7 to 10 days or loss of visual acuity: orbital decompression may be necessary.
- For diplopia: Correction of eye muscle by surgery (but should be delayed for 6 months, until degree of diplopia is stable).

N.B.: For details, see in the chapter 'Examination of the eye'.

Remember, ophthalmopathy in Graves disease:

- Eye problems occur in 5 to 10% of cases.
- Ophthalmopathy occurs in 50% in the first presentation, may develop after treatment of hyperthyroidism and precedes many years before hyperthyroidism.
- If hypothyroidism develops, exophthalmos may be aggravated, especially if treated with radioiodine therapy.
- Lid retraction resolves when the patient is euthyroid, but exophthalmos resolves slowly and may take up to 2 to 3 years.

Q: Is there any evidence of **cancer** in Graves disease?

A: Unusual, but highly suspicious if there is associated cold nodule.

Eponyms of eye signs in thyroid disease:

- Lid lag of upper eyelid: Von Graefe's sign.
- Lid lag of lower eyelid: Griffith's sign.
- Lid retraction: Dalrymple's sign.
- Absence of wrinkling of forehead on upward gaze: Joffroy's sign.
- Impaired convergence of eye: Möbius' sign.
- Infrequent blinking: Stellwag's sign.
- Paralysis of extraocular muscles: Jendrassik's sign.
- Weakness of at least one extraocular muscle: Ballet sign.
- Tremor of closed eyelids: Rosenbach's sign.

Q: What is malignant exophthalmos?

A: It is the severe, progressive exophthalmos, which may lead to blindness due to optic nerve compression. Treated with high dose of prednisolone up to 120 mg/day. It may require decompression or orbital irradiation.



Malignant exophthalmos
(with chemosis)



Exophthalmos (less severe)



Malignant exophthalmos with
peri-orbital oedema

Q: What is pretibial myxoedema (dermopathy)?

A: It is characterized by firm, nodular, thickened or plaque like lesion, pink or brown colour giving a peau d'orange appearance, due to the deposition of mucopolysaccharide in the dermis. Usually, present in the shin of legs up to the dorsum of foot (but may occur in any part of the body, especially at pressure point). It may be pruritic and hyperpigmented, found only in Graves disease in 10%, almost always associated with ophthalmopathy and is not a manifestation of hypothyroidism (pretibial myxoedema is a misnomer). Occasionally, pretibial myxoedema develops after treatment with radioiodine therapy.



Pretibial myxoedema (in shin)



Pretibial myxoedema (in dorsum of leg)

Treatment is rarely necessary. Local injection of triamcinolone or ointment betamethasone may be helpful.

GOITRE

Instruction by the examiner:

- Examine the neck or examine the thyroid gland and see the relevants.

Usual cases in the examination are—

- Single simple nodular goitre.
- Single toxic nodular goitre.
- Simple multinodular goitre.
- Toxic multinodular goitre.
- Simple diffuse goitre.
- Toxic diffuse goitre.
- Malignant goitre.

Examine systematically in the form of inspection, palpation, percussion and auscultation. Finally, see the features of thyroid function (toxic or hypothyroid features) as described above in introduction.

SIMPLE NODULAR GOITRE (SOLITARY NODULE)

Presentation of a Case:

- There is a nodular goitre involving right lobe (or left lobe), 2×2 cm, firm in consistency, non-tender, smooth surface, freely movable, no bruit and no palpable lymph node.
- No signs of toxicosis.

My diagnosis is **Simple nodular goitre** (or solitary thyroid nodule).

Q: Why this is **simple** nodular goitre?

A: Because, there is no sign of toxicosis.

Q: What are the **causes or differential diagnosis** of solitary thyroid nodule?

A: As follows:

- Simple nodular goitre.
- Palpable nodule on diffuse or multinodular goitre.
- Thyroid cyst.
- Thyroid adenoma.
- Toxic adenoma (Plummer's disease).
- Malignancy (carcinoma or lymphoma).

Q: What is the **nature** of solitary nodule?

A: Majority benign (80 to 90%) and some cases may be malignant (5 to 10%).

Q: Mention **one investigation**.

A: USG of thyroid.



Solitary nodule (right lobe)



Solitary nodule (isthmus)



Solitary nodule (left lobe)

Q: What **investigations** do you suggest?

A: As follows:

- USG (to see whether cystic or solid).
- RAIU and thyroid scan.
- FT_3 , FT_4 and TSH.
- FNAC.

N.B.: FNAC is the investigation of choice for single thyroid nodule, accuracy is 70 to 97%.

Q: How to **treat** solitary thyroid nodule?

A: As follows:

1. 80% of the thyroid nodules are solid, cold, non-toxic and colloid. Treatment is as follows:
 - Reassurance and follow up.
 - Surgery for cosmetic purpose or if suspicion of malignancy.
 - Thyroxine may be given in some cases.
2. 5 to 10% of the thyroid nodules are hot nodules. Treatment is as follows:
 - Surgery or radioiodine therapy.
 - Ethanol injection into the nodule may be given.
3. Cystic nodule is usually benign. Aspiration is effective in 50% cases. Ethanol injection into the nodule is helpful. Thyroxine therapy is ineffective. Large cyst (>4 cm) or cyst with bloody fluid usually recur and surgical excision should be considered.

Q: What are the **types** of benign adenoma?

A: 3 types:

- Follicular (commonest).
- Papillary.
- Hurthle cell type.

Q: How to **treat** benign adenoma?

A: As follows:

- If non-functioning: Reassurance and follow-up.
- Thyroxine may be given (if <4 cm, FNAC shows benign lesion and no risk factor for malignancy). Dose 2 to 3 mg/kg/day for 6 months. Then, re-evaluate. If no response, stop the therapy.
- Surgery: For cosmetic purpose or suspicion of malignancy.

Q: What is **toxic adenoma**?

A: Thyrotoxicosis due to thyroid adenoma (usually follicular), also called Plummer's disease (no eye sign and no pretibial myxoedema). Thyroid scan shows hot nodule. It occurs in 5% cases of hyperthyroidism, common in females of >40 years.

Treatment: Radioiodine therapy or surgery.

Q: How to **suspect malignancy** in a single thyroid nodule?

A: As follows:

- Elderly.
- History of recent and rapid growth.
- Hoarseness of voice.
- History of radiation therapy in childhood (in head and in neck).
- Family history (medullary carcinoma of thyroid).
- Gland is solitary, hard, irregular and fixed to the underlying structures.
- Associated palpable lymph node.

Q: What are the **types of nodules** seen in thyroid scan?

A: 2 types:

1. Non-functioning: Cold nodule.
2. Functioning:
 - Hot nodule: Only functioning nodule takes radioiodine, other parts of thyroid are suppressed.
 - Warm nodule: Functioning nodule and part of surrounding nodule show uptake.
 - Isofunctioning nodule and other parts of surrounding nodule show equal uptake and both cannot be differentiated.

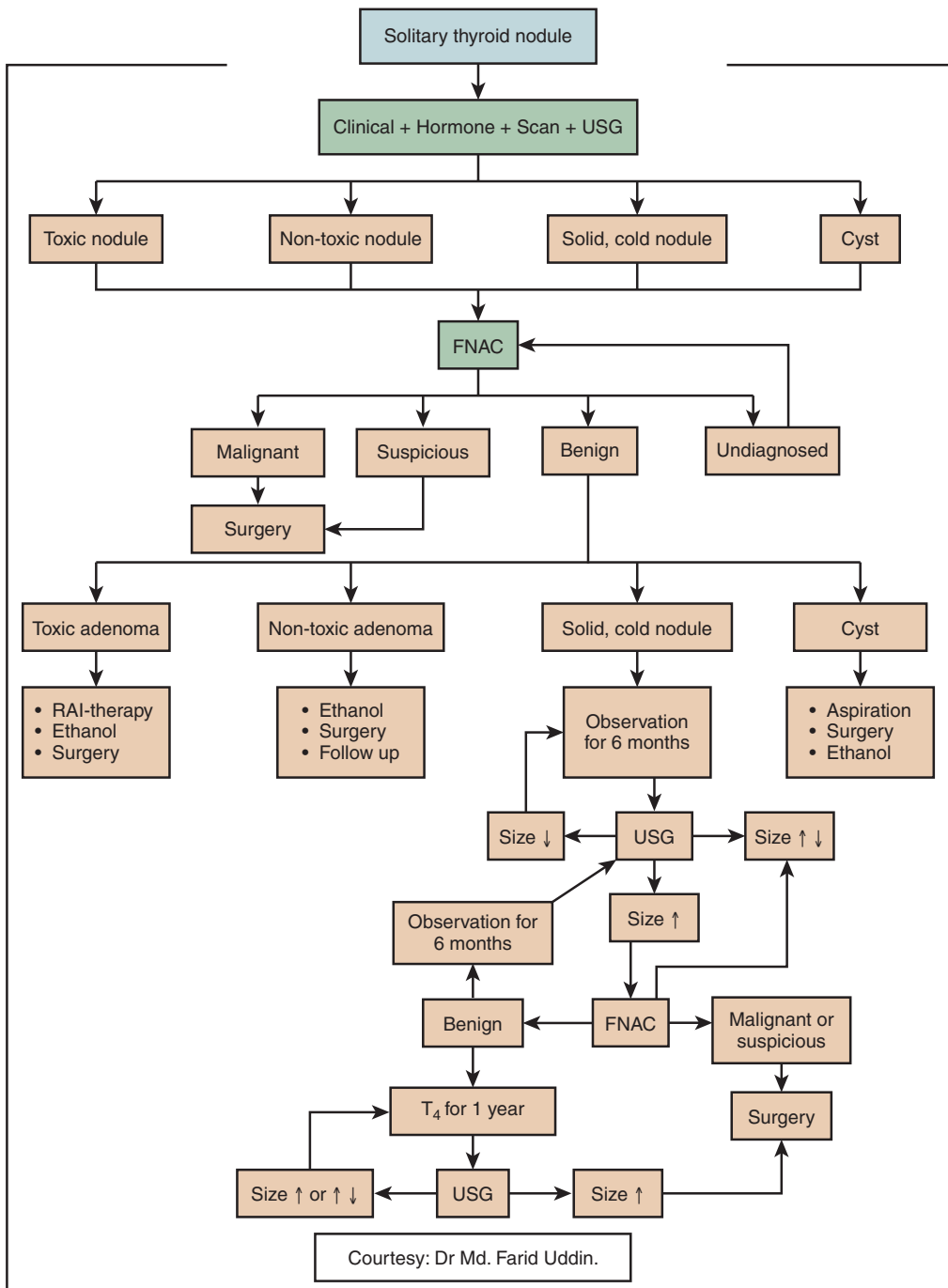
Q: How to **treat** functioning nodule?

A: As follows:

1. Hot nodule:
 - Radioiodine therapy: Better, especially after 40 years of age.
 - Surgery.
 - Local injection of alcohol: 1 to 2 mL weekly, 4 to 8 injections (80 to 90% effective).
2. Warm nodule: Follow-up. Local injection of alcohol may be considered.
3. Isofunctioning nodule: Follow-up. Local injection of alcohol may be considered.

Q: How would you **investigate** a patient presenting with solitary thyroid nodule?

A: See the scheme below:



Q: What is the **fate** of untreated thyroid nodule?

A: As follows:

- May persist for long time.
- Spontaneous regression in 30%.
- Malignancy (5 to 10%).
- Cystic changes due to haemorrhage within the nodule.
- Secondary infection.

SIMPLE MULTINODULAR GOITRE

Instruction by the examiner:

- Examine the neck or Examine the thyroid gland and relevant.

Presentation of a Case:

- There is multinodular goitre, left lobe is larger than the right, nodules are of variable size and shape, non-tender, firm in consistency and freely movable.
- There is no bruit, no retrosternal extension and no cervical lymphadenopathy.
- The patient is clinically euthyroid (pulse—normal, no tremor, no warm and sweaty palm).

My diagnosis is **Simple multinodular goitre**.

Q: Why this is **simple**?

A: Because, no features of thyrotoxicosis such as no tachycardia, no tremor of outstretched hand, no warm and sweaty palm.

Q: What are the **causes of simple multinodular goitre**?

A: As follows:

- Iodine deficiency (commonest cause).
- Drugs: Lithium, amiodarone and para-aminosalicylate (PAS).
- Thiocyanate in diet.

Q: How to **investigate a multinodular goitre**?

A: As follows:

- RAIU test, usually normal. In iodine deficiency, there is high uptake and slow turnover.
- Thyroid scan.
- USG of thyroid gland.
- FT₃, FT₄ and TSH (all normal. TSH may be high, due to iodine deficiency).
- FNAC of thyroid nodule.
- In iodine deficiency, measurement of urinary iodine (<10 mg/dL) may be done.



Multinodular goitre (small size)



Multinodular goitre (huge)



Multinodular goitre (huge)

Q: What are the complications of multinodular goitre?**A:** As follows:

- May develop thyrotoxicosis (toxic multinodular goitre).
- Compression: Such as dysphagia, hoarseness (due to involvement of recurrent laryngeal nerve), stridor and superior vena cava obstruction.
- Severe pain due to haemorrhage in nodule.

Q: How to treat?**A:** As follows:

- If small: Reassurance. Follow-up annually.
- If large or mediastinal compression or cosmetic reason: surgery.

N.B. Remember the following points in multinodular goitre:

- Common in middle aged and elderly.
- Usually it is benign, chance of malignancy is rare. Malignancy may occur, if cold nodule.
- Thyroxine therapy: Not much effective and may cause toxicosis.

TOXIC NODULAR OR MULTINODULAR GOITRE**Instruction by the examiner:**

- Examine the neck or examine the thyroid gland and relevants.

Presentation of Case No. 1

- There is nodular goitre involving the right lobe of thyroid, which is 3×2 cm in size, firm in consistency, non-tender, smooth surface, freely movable, no bruit and no palpable lymph node.
- Signs of toxicosis are present (tachycardia, tremor of outstretched hand, warm and sweaty palm).

My diagnosis is **Toxic nodular goitre**.

Presentation of Case No. 2

- There is multinodular goitre, involving both lobes, nodules are of variable size and shape, non-tender, firm in consistency and freely movable.
- Signs of toxicosis are present (tachycardia, tremor of the outstretched hand, warm and sweaty palm).

My diagnosis is **Toxic multinodular goitre**.

Q: What is the **natural history** of toxic multinodular goitre?

A: It is permanent and usually there is no spontaneous remission.

Q: How to **investigate** such a case?

A: As follows:

- FT₃, FT₄ and TSH (high T₃ and T₄, low TSH).
- RAIU test and thyroid scan (shows rapid uptake and rapid turnover, high uptake after 2 and 24 hours, falls after 48 hours).
- USG of thyroid gland.
- Other tests (as described in thyrotoxicosis, such as ECG, chest X-ray, antithyroid antibody etc.).

Q: How to **treat** toxic nodular or multinodular goitre?

A: As follows:

- β -blocker (to reduce heart rate).
- Radioiodine therapy is the treatment of choice (high dose: 15 to 30 mCi). If severe toxicosis, antithyroid drug is given, followed by radioiodine therapy.
- Occasionally, surgery, if large goitre. However, before surgery, patient should be made euthyroid.

N.B. Antithyroid drugs are given for short time. Long term treatment with antithyroid drug is not helpful, as many nodules are autonomous and relapse is invariable after withdrawal of the drug.

Q: What are the **difference** between Graves disease and toxic multinodular goitre?

A: As follows:

Features	Graves Disease	Toxic Multinodular Goitre
1. Age	20 to 40 years	Middle aged or elderly
2. Past history	Not specific	Nodular goitre for long time
3. Thyroid gland	Diffusely enlarged	Multinodular goitre
4. Cause	Autoimmune disease	Usually iodine deficiency
5. Ophthalmopathy	Common	Rare
6. Dermopathy	Common	Absent
7. Heart complications	Less common	More common
8. Thyroid acropachy	May occur	Absent
9. Hypothyroidism	May occur	Absent

SIMPLE DIFFUSE GOITRE

Instruction by the examiner:

- Examine the neck or, examine the thyroid gland and relevants.

Presentation of a Case:

- Thyroid gland is diffusely enlarged, 5×4 cm, non-tender, firm in consistency, freely mobile, no bruit, no retrosternal extension and no palpable lymph node.
- There are no signs of toxicosis.

My diagnosis is **Simple diffuse goitre**.

Q: Why is it simple?

A: Because there are no signs of toxicosis (see above). However, if features of toxicosis, then tell **Diffuse toxic goitre**.

Q: What do you think are the causes in this case?

A: As follows:

- Iodine deficiency.
- If the patient is young, it may be puberty goitre.
- Goitrogens.

Q: What are the presentations of simple diffuse goitre?

A: It is common in the 2nd and 3rd decade, 15 to 25 years, more in females (F:M = 3:1). The patient presents with swelling in the neck. Or only goitre is found during routine examination. Sometimes, goitre is evident in pregnancy.



Diffuse goitre (simple)



Puberty goitre (simple)



Diffuse goitre (simple)

Q: What are the **causes** of diffuse goitre?

A: As follows:

- Physiological: Puberty and pregnancy.
- Iodine deficiency (endemic goitre).
- Autoimmune: Hashimoto thyroiditis, Graves disease and post-partum thyroiditis.
- Goitrogens: Drugs (amiodarone, lithium, para-aminosalicylate). Thiocyanate in diet (cabbage, cauliflower, turnips, soya beans, Brussels, sprouts).
- Iodide intake in large doses.
- Subacute thyroiditis (de Quervain's thyroiditis).
- Dys hormonogenesis.
- Riedel's thyroiditis.
- Suppurative thyroiditis.
- Infiltrative disease: Amyloidosis and sarcoidosis.

Q: How to **treat** simple diffuse goitre?

A: As follows:

- Mild to moderate: Reassurance and follow up. T₄ is sometimes helpful to shrink goitre. Treatment of primary cause.
- Large goitre with pressure effect or cosmetic reason: surgery may be done.

N.B. Clue for the diagnosis of different types of goitre:

- *Diffuse and soft goitre, with exophthalmos: Suggestive of Graves disease.*
- *Diffuse and firm, rubbery or hard goitre, with no exophthalmos: Suggestive of Hashimoto's thyroiditis.*
- *Diffuse and soft: Suggestive of simple diffuse goitre.*
- *Diffuse, soft and tender: Suggestive of subacute thyroiditis.*

THYROID MALIGNANCY

Presentation of Case No. 1

- There is nodular goitre involving the right lobe of thyroid, which is 5×3 cm in size, hard in consistency, non-tender, surface is irregular, fixed with the underlying structure, no palpable lymph node (or palpable, mention if present).
- Signs of toxicosis are absent.

My diagnosis is **Nodular goitre, likely to be malignant.**

Q: Why it is malignant?

A: Because it is hard, irregular surface and margin, fixed with the underlying structure.

Q: What are the types of thyroid malignancy?

A: Thyroid carcinoma is less common, 1% of the malignancies. Usually, thyroid malignancy is associated with euthyroidism, occasionally hyperthyroidism. All are common in females except MCT, which occurs equally in both sexes. Types are:

- Papillary: 70 to 80% (commonest).
- Follicular: 10%.
- Anaplastic or undifferentiated: 5%.
- Medullary carcinoma of thyroid (MCT): 5 to 10%.
- Others: 5% (lymphoma, rarely secondary deposit in thyroid).

PAPILLARY CARCINOMA

Features are:

- Commonest type, usually in young, 20 to 40 years female. May occur in later life (bimodal).
- It is slowly growing, multifocal, 90% of irradiation induced thyroid cancer.
- Local lymph node metastasis is common, haematogenous spread is less common.
- Patient may present with cervical lymphadenopathy without thyroid enlargement.
- FNAC is very sensitive and specific test.

Treatment and prognosis:

- Total thyroidectomy followed by high dose (100 mCi) radioiodine therapy (to ablate remaining thyroid tissue and metastatic site). However, recent data indicates that 30 mCi radioiodine may be equally effective.
- Lifelong thyroxine (to suppress TSH, as it is TSH dependent).
- Prognosis is good, survival is almost the same as in normal person, if the lesion is localized. 20 years survival in 95% (so, it is potentially benign lesion).
- If distant metastasis, 40% survival up to 10 years.

Follow-up (following tests are done periodically):

- Serum thyroglobulin. If raises, indicates recurrence or metastasis (normally, thyroglobulin is undetectable).
- Measurement of thyroglobulin is most sensitive when TSH is high, so thyroxine may be stopped for 4 to 6 weeks or recombinant TSH 900 µg IM (2 doses over 48 hours) may be given to stimulate thyroglobulin.
- If there is recurrence, high dose radioablation should be done.
- Oral sorafenib has a good short-term response in locally advanced and metastatic differentiated thyroid cancers that are refractory to radioiodine.
- Periodic whole body scanning is done to check any metastasis. USG, CT or MRI may be done to detect metastases.

FOLLICULAR CARCINOMA

Features are:

- Common in middle aged female, 40 to 60 years of age.
- Usually, a single encapsulated lesion.
- Blood borne metastasis is common (to lung, brain and bone).
- Lymph node metastasis is rare.

Diagnosis:

- Open biopsy should be done (FNAC is less specific).

Treatment and follow-up:

- Exactly like papillary.
- Both follicular carcinoma and its secondary metastasis takes up and responds to radio-iodine therapy.
- Prognosis is good.

LYMPHOMA OF THYROID

Features are:

- Rarely, may occur as primary or as a part of generalized lymphoma.
- Generally occurs in thyroid gland affected by Hashimoto's thyroiditis, better prognosis with median survival of 9 years.
- A rapidly enlarging mass in thyroid in patients with Hashimoto's thyroiditis should arouse suspicion of lymphoma.
- 98% are non Hodgkin's type, usually the diffuse large B-cell subtype.

Treatment:

- External beam irradiation plus chemotherapy.

ANAPLASTIC OR UNDIFFERENTIATED CARCINOMA

Features are:

- Usually in the elderly, >60 years, more in women and highly malignant.
- Rapid thyroid enlargement over 2 to 3 months. Goitre is hard.
- There may be hoarseness of voice due to recurrent laryngeal nerve involvement and stridor due to tracheal compression.

Treatment:

- If possible, surgery (total thyroidectomy and thyroxine therapy).
- Resistance to almost any other treatment.
- Radiotherapy may be given.

Prognosis:

- Survival is 7 months after diagnosis, if surgery is not possible.

MEDULLARY CARCINOMA OF THYROID (MCT)

Features are:

- Medullary thyroid carcinoma is a neuroendocrine tumour of calcitonin producing parafollicular C cells of thyroid.
- Usually multifocal. May be inherited as autosomal dominant disease.
- Common in middle aged and elderly, but may occur in young age if there is family history.
- Associated with multiple endocrine neoplasia (MEN) type-IIa (phaeochromocytoma and hyperparathyroidism) and -IIb (as in type-IIa plus multiple neuroma and Marfanoid body). May be sporadic also.
- Serum calcitonin is high (but no hypocalcaemia) and CEA may be high.
- Also secretes histamine, serotonin, slow reacting substance of anaphylaxis (SRS-A), prostaglandin and ACTH.
- May cause carcinoid syndrome and Cushing's syndrome.
- Cervical lymph node metastasis is common and haematogenous spread is rare.

Treatment:

- Total thyroidectomy with removal of affected lymph nodes and thyroxine therapy.
- External beam radiotherapy may be given after surgery in some patients at high risk of local recurrence.
- Does not take radioiodine. Chemotherapy is not effective.
- Local invasion or metastasis is frequent, and the tumour responds poorly to treatment, although progression is often slow.
- Recently, biological therapy with vandetanib and cabozantinib have shown benefit in advanced medullary thyroid carcinoma.

Prognosis:

- Variable and relatively good. Some may survive up to 20 years, but some <1 year.
- Individuals can live for many decades with persistent disease which behaves in an indolent fashion.

ACROMEGALY

Instruction by the examiner:

- Look at the patient. What is the diagnosis? What else do you want to examine?
- Examine the hands of the patient. What is your diagnosis?
- Perform the general examination of the patient.

Presentation of a Case (By Looking at the Patient): Case No. 1

- Skull enlarged (look for any frontal craniotomy scar).
- Large coarse facies with prominent supraorbital ridge, more wrinkling of forehead and baggy eyelids.
- Large jaw with prognathism (protrusion of lower jaw forward), large lips, nose and ears.
- Teeth show malocclusion, widely apart, lower teeth overbites the upper teeth.
- Tongue is large (macroglossia).

My diagnosis is Acromegaly.

Q: What else do you want to examine in this case?

A: As follows:

- Hands (shake hands): See below (case no. 2).
- Legs: Large feet.
- Eyes: Bitemporal hemianopia (see visual field).
- Skin: Thick, greasy and sweaty.
- Other parts of body: Enlarge as a whole.
- Talk with the patient: Husky and cavernous voice (due to the enlargement of larynx).
- Axilla: Acanthosis nigricans and skin tag (molluscum fibrosum).
- Others: Kyphosis, arthritis, gynaecomastia, coarse hair, cardiomegaly and thyromegaly.
- Check BP (high).
- Examine the urine for sugar (secondary DM may occur).



Acromegaly



Large face, jaw, lips



Spade-like hands

Presentation of a Case (By Examining the Hands): Case No. 2

- Both hands are large, warm and sweaty, doughy feeling, spade like fingers.
- Carpal tunnel syndrome (if asked to examine the hands, always test for it).
- Clubbing involving all the fingers is present.

My diagnosis is **Acromegaly**.



Large foot



Widely apart teeth with prognathism (front view)



Prognathism (side view)

Presentation of a Case (General Examination): Case No. 3

- Whole body looks enlarged including skull, tongue, hands, feet.
- Large jaw with prognathism (protrusion of lower jaw forward), large lips, nose and ears.
- Teeth show malocclusion, widely apart, lower teeth overbites the upper teeth.
- Clubbing involving all the fingers is present.
- Enlargement of breasts.
- BP is high.

My diagnosis is **Acromegaly**.

Q: What is the possible **differential diagnosis**?

A: Hypothyroidism.

Q: What **else** do you want to see?

A: I want to talk with the patient, to see any change in voice. Also, I want to see the visual fields.

Q: What are the **changes** in the eyes in acromegaly?

A: Bitemporal hemianopia (due to pressure on optic chiasma). Also, optic atrophy, papilloedema and angioid streaks in retina.

Q: What is **acromegaly**?

A: Acromegaly is characterized by generalized enlargement of the whole body. It is due to excess growth hormone secretion from pituitary macroadenoma (>10 mm) after union of epiphysis. If occurs before the union of epiphysis, it is called gigantism.

Q: Why it is called acromegaly?

A: Because of the enlargement of peripheral (acral) parts of body (*acro* means periphery or limbs and *megaly* means big).

Q: Can acromegaly and gigantism exist together?

A: Yes, if excess growth hormone starts in adolescence and persists in adult life, the two conditions may be present together.

Q: What is the cause of acromegaly?

A: Eosinophilic adenoma of pituitary (macroadenoma) causing excess growth hormone (GH) secretion after fusion of epiphysis. Rarely, ectopic production of growth hormone releasing hormone (GHRH) may cause acromegaly (in pancreatic islet cell tumour, oat cell carcinoma of bronchus and medullary carcinoma of thyroid).

Q: What are the causes of prominent supra-orbital ridge?

A: As follows:

- Rickets.
- Paget's disease.
- Achondroplasia.
- Hydrocephalus.
- Hereditary haemolytic anaemia.

Q: What are the causes of macroglossia?

A: As follows:

- Acromegaly.
- Hypothyroidism.
- Amyloidosis.
- Down's syndrome.
- Cretinism.
- Hurler's syndrome.

Q: What are the causes of baggy eyelids?

A: As follows:

- Old age.
- Myxoedema.
- Acromegaly.
- Alcoholism.
- Nephrotic syndrome or acute glomerulonephritis.



Gigantism

Q: What are the signs of active acromegaly?**A:** Signs of activity:

- Progressive increase in body size.
- Excessive sweating.
- Increasing visual field defect.
- Large skin tags (Molluscum fibrosum).
- Presence of glycosuria (DM).
- Hypertension.
- Progressive headache.
- Enlarging thyroid.

Q: What are the presentations of acromegaly?**A:** As follows:

- Progressive increase in body size (may be history of change in size of rings, shoes, hats).
- Weight gain but weakness.
- Visual field defect (patient gives history of collision with doors, persons because of defective temporal field of vision).
- Headache (common).
- Excessive sweating.
- Features of hypertension, DM.
- Patient may give history of frequent visit to the dentist due to dental problems.
- Sleep apnoea syndrome.
- Amenorrhoea or oligomenorrhoea in women.
- Impotence or decreased libido.
- Galactorrhoea.

Q: What are the long term complications of acromegaly?**A:** Increased incidence of large bowel carcinoma and increased atherosclerosis.**Q: What are the causes of death in acromegaly?****A:** As follows:

- Heart failure.
- Complications of hypertension.
- Degenerative vascular disease.
- Tumour expansion (mass effect).
- Pituitary apoplexy: Rapid expansion of pituitary tumour due to infarction or haemorrhage within the tumour. The patient complains of sudden severe headache and loss of consciousness (require immediate neurosurgical intervention).

Q: What investigations should be done in acromegaly?**A:** As follows:**1. Radiology:**

- Skull X-ray: It shows enlarged sella turcica, erosion of clinoid process, enlarged skull, mandible and sinuses.
- X-ray of the hands: There is large soft tissue, bones, widening of joint space and tufting of terminal phalanges.
- X-ray of the foot: To see heel pad (normally, in male up to 21.5 mm and in female 18 mm. If >25 mm, highly suggestive). Other changes like hand.
- Other X-rays: Knee joint and chest X-ray.

2. GH assay (radioimmunoassay): Normally, <1 mU in adult (except in stress).
3. GTT with simultaneous measurement of GH (more diagnostic): Normally during GTT, there is suppression of GH <2 mU. In acromegaly, there is failure of suppression of GH, may be paradoxical rise of GH.
4. Measurement of IGF-1 (also called somatomedin-C): usually increases.
5. CT scan or MRI of the skull (MRI is more preferable).
6. Others:
 - Assessment of other anterior pituitary hormones. Serum prolactin (high).
 - Comparison with old photographs.
 - Perimetry (to see bitemporal hemianopia).
 - Blood sugar: DM in 10% cases, IGT in 25% cases.
 - ECG.
 - Serum calcium (increases in MEN).
 - Colonoscopy may be done (incidence of large bowel carcinoma is high).

Q: What are the **treatments** for acromegaly?

A: Treatment options are surgery, radiotherapy, drug therapy.

1. Surgery:
 - Trans-sphenoidal removal of pituitary tumour (high success rate, rapid reduction of growth hormone and low incidence of hypopituitarism). Cure rate is 60 to 90% in microadenoma and 50% in macroadenoma.
 - After 3 months post-operative, measure growth hormone and pituitary function tests. If growth hormone remains high, adjuvant medical or radiotherapy may be needed.
 - Occasionally, trans-frontal surgery is done in large macroadenoma with suprasellar extension. Total removal of tumour may not be possible due to more complications. Post-operative radiotherapy should be given.
2. Radiotherapy:
 - It is used as a second line therapy. External irradiation by linear accelerator is given, when the tumour persists after surgery, to stop the tumour growth and to lower growth hormone levels. However, growth hormone level falls very slowly over many years (previously implantation of Yttrium was used).
 - Radiotherapy can be used in combination with somatostatin analogue or dopamine agonist because of slow biochemical response to radiotherapy.
 - Stereotactic (gamma-knife) radiotherapy may be used (it delivers more concentrated field of radiation).
3. Drugs: Given if surgery is not possible or persistent acromegaly after surgery.
 - Somatostatin analogue (octreotide or lanreotide) may be used as a slow-release injection, every 2 to 4 weeks.
 - Bromocriptine: It is a dopamine agonist, given in high dose, which reduces GH level and the size of tumour. But it is less potent in lowering growth hormone and recurs after withdrawal of drug. Its main side effects are nausea, vomiting and postural hypotension. Alternatively, cabergoline 0.5 mg/day or quinagolide may be used.
 - A peptide GH receptor antagonist (pegvisomant) may be used.
4. Other treatment:
 - Control of hypertension and DM (both improve with the treatment of acromegaly).
 - Cardiac problems: Whether it improves with the treatment of acromegaly is not clear.

N.B. Aim of treatment is to reduce GH level below 5 mU/L. A normal IGF-1 level is also a goal of therapy.

Q: How to assess the **response of therapy** in acromegaly?

A: As follows:

- Clinical improvement (decreased facial puffiness, body size, less sweating, improvement of hypertension and DM).
- Progress can be assessed by GH and IGF-1 measurement.

Q: What are the **complications** of acromegaly?

A: As follows:

- Hypertension.
- Cardiomegaly.
- DM, IGT.
- Visual field defect.
- Hypopituitarism.
- Neoplasia (colonic polyp, carcinoma, uterine leiomyoma).
- Arthritis.

BRIEF DISCUSSION ABOUT HYPERPROLACTINAEMIA

Q: What are the **causes of hyperprolactinaemia**?

A: As follows:

1. Physiological: Severe stress, pregnancy, lactation, exercise, coitus and sleep.
2. Drugs:
 - Dopamine antagonist group of drugs:
 - Antipsychotic (phenothiazine, butyrophenones).
 - Antiemetic (metoclopramide, domperidone).
 - Antidepressant.
 - Dopamine-depleting drugs (methyldopa).
 - Oestrogen therapy (e.g., oral contraceptive pill).
 - Others: verapamil, cimetidine.
3. Pathological:
 - Prolactinoma (usually microadenoma <10 mm).
 - Pituitary macroadenoma.
 - Primary hypothyroidism.
 - Polycystic ovarian syndrome.
 - Rarely: Renal failure, liver failure, hypothalamic tumour, ectopic tumour, post-ictal state, chest wall injury (e.g., post herpes zoster).
 - Idiopathic.
 - Macroprolactinaemia (there is high prolactin without clinical features of hyperprolactinaemia).

Clinical features of hyperprolactinaemia:

- Galactorrhoea, hypogonadism (commonest symptoms).
- In male: Decreased libido, impotence, lethargy, mild gynaecomastia.
- In female: Amenorrhoea, oligomenorrhoea, menorrhagia, infertility.
- Osteoporosis in chronic case.

Investigations:

- Serum prolactin (very high).
- CT or preferably MRI of brain.
- Anterior pituitary function should be assessed.
- Visual field should be checked.
- Other investigations according to the suspicion of cause, e.g., thyroid function, renal function.

N.B. Remember the following points:

- *If serum prolactin is high, repeat measurement is indicated to reconfirm.*
- *If serum prolactin is in the range of 500–1000 mU/L, it is more likely due to stress or drugs.*
- *If serum prolactin is in the range of 1000–5000 mU/L, it may be due to stress or drugs or microadenoma.*
- *Serum prolactin >5000 mU/L is highly suggestive of macroprolactinoma.*

Treatment:

- Treat the primary cause and stop the responsible drugs, if any.
- Dopamine agonist (such as bromocriptine, cabergoline and quinagolide) are usually given as a first-line therapy.
- Trans-sphenoidal surgery: May be done in microadenoma (cure rate is about 80%, may recur). It is also done in macroadenoma, though complete removal may not be possible with risk of pituitary damage.
- Radiotherapy: If macroadenoma fails to shrink following dopamine agonist drugs or total surgical removal is not possible.
- In pregnancy, tumour size may be enlarged, may cause headache and visual field defect. In such case, dopamine agonist therapy (usually bromocriptine) should be started, if there are symptoms.

Indications of surgery:

- Intolerance to drugs.
- Resistance to drugs.
- Rapid expansion of tumour causing mass effect like visual field defect.
- Large cystic macroadenoma.

CUSHING'S SYNDROME

Instruction by the examiner:

- Perform the general examination of this patient.
- Look at the face. What are your findings? What else do you want to examine? Describe the face as written below. Then mention, 'I want to examine neck (see below), abdomen (striae), proximal myopathy, bony pain due to osteoporosis, BP and urine for sugar test'.
- Look at the abdomen or thigh or arm. What are your findings? What else do you like to examine?

Presentation of a Case (General Examination): Case No. 1:

- The patient is obese. There is truncal obesity with relatively lean and thin limbs (**lemon on a match stick appearance**).
- There is deposition of fat at the root of neck (buffalo hump and increased fat above the supraclavicular fossa).
- Face is moon-like, puffy, plethoric with acne and hirsutism.
- There are multiple pink or purple striae in abdomen and other parts (thigh, arm).
- Skin is thin, with multiple purpura or bruise.
- Proximal myopathy is present.
- There is kyphosis or scoliosis and tenderness in spine (due to osteoporosis).
- BP is high.

My diagnosis is **Cushing's syndrome**.

Q: What **history** do you like to take? Or ask one **question** to the patient.

A: I want to know about prolonged use of steroid.

Q: What are your **differential diagnoses**?

A: As follows:

- Simple obesity.
- Hypothyroidism.
- Metabolic syndrome.
- Polycystic ovarian syndrome (in early age).



Plethoric moon face with stria on arm



Hirsutism and plethoric moon face



Buffalo hump—left arrow, supraclavicular fat right arrow, hirsutism

Presentation of a Case (Looking at Face): Case No. 2:

- Face is moon-like, puffy, plethoric with acne and hirsutism.

Q: What is the likely **diagnosis**?

A: Cushing's syndrome.

Q: What **else** do you want to see or examine?

A: I want to examine neck (to see buffalo hump, supraclavicular fat deposition), striae (in different parts of the skin), proximal myopathy, bony pain due to osteoporosis, BP and urine for sugar test.

Q: What are the causes of **moon face** or **puffy face**?

A: As follows:

- Simple obesity.
- Cushing's syndrome (plethoric moon face, with hirsutism, acne).
- Myxoedema (puffy with baggy eyelids, fall of lateral eyebrows, malar flush).
- Nephrotic syndrome and acute glomerulonephritis (puffy with periorbital oedema).
- Superior vena caval obstruction (engorged and nonpulsatile veins, plethoric face with subconjunctival effusion).
- Angioedema (localized, swollen lip or face).
- Chronic alcoholism (plethoric, puffy face).
- Surgical emphysema (history of trauma, also swelling is extended up to the neck and chest. There are multiple crepitations on palpation).

Presentation of a Case (Looking at the Abdomen or Thigh). Case No. 3:

- There are multiple pink or purple striae in abdomen and other parts (thigh, arm).

Q: What is the likely **diagnosis**? Why?

A: Cushing's syndrome. Because face is puffy, plethoric, moon-like. The patient looks obese with gynaecomastia.

Q: What are the **other skin changes**?

A: Skin is thin, with multiple purpuric spot, bruise or ecchymosis.

Q: What **else** do you like to **examine** in this patient?

A: Mention as above.

Q: What **bedside investigation** will you do?

A: I want to examine the urine for sugar.

Q: What is the commonest **cause** of Cushing's syndrome?

A: Prolonged use of steroid.



Cushing's syndrome
(large breast, striae)



Striae in thigh



Striae in abdomen

Q: Name some diseases where **steroid** is used for prolonged period.

A: Addison's disease, SLE, pemphigus vulgaris, dermatomyositis, severe rheumatoid arthritis, hypopituitarism, diffuse parenchymal lung disease (DPLD) etc.

Q: Mention one **absolute indication of steroid therapy**.

A: Pemphigus vulgaris (also Addison's disease).

Q: Why **backache** in Cushing's syndrome?

A: Osteoporosis (may cause vertebral collapse and kyphosis).

Q: What is the character of **striae** in Cushing's syndrome?

A: Striae are pink or purple coloured in the skin of abdomen and other parts of body.

Q: What are the **eye complications** in Cushing's syndrome?

A: Cataract.

READ THE FOLLOWING TOPICS IN RELATION TO CUSHING'S SYNDROME

Q: What is **Cushing's syndrome**? What are the common **features**?

A: It is defined as constellation of symptoms and signs characterized by prolonged glucocorticoid excess due to any cause. Common features are:

- Weight gain but weakness, lethargy.
- Proximal muscular weakness (characterized by difficulty in combing, raising hands above head, standing from squatting).
- Backache, pathological fracture (due to osteoporosis), collapse of the vertebra with reduction of height.
- Easy bruising, purple striae.
- In female: Amenorrhoea or oligomenorrhoea, hirsutism.
- Loss of libido.
- Frequent infection, especially fungal infection, slow wound healing.
- Hypertension, DM (30%) or IGT.
- Mood disturbance such as depression, insomnia, irritability.
- On examination: Moon face, buffalo hump, truncal obesity, hirsutism, acne on face, pink striae, growth retardation in children.

Q: What is the **difference** between Cushing's disease and Cushing's syndrome?

A: As follows:

- Cushing's disease shows increased ACTH from pituitary gland that stimulates adrenals, causing excess cortisol secretion.
- Cushing's syndrome is caused by excess steroid due to any cause.

Q: What are the **causes** of Cushing's syndrome?

A: Commonest cause is steroid therapy for long time. Other causes are:

1. ACTH dependent:
 - Pituitary microadenoma <10 mm called Cushing's disease (80%). Common in women.
 - Ectopic ACTH syndrome (oat cell carcinoma of bronchus, bronchial adenoma, bronchial carcinoid, carcinoma of pancreas).
 - ACTH therapy.
2. Non-ACTH dependent:
 - Steroid therapy: commonest cause (even topical or inhaled steroid for long time in susceptible cases may be responsible).
 - Adrenal adenoma and adrenal carcinoma (common in women).
3. Others: Pseudo-Cushing's syndrome (due to alcohol, depression and obesity).

Q: What is **Pseudo-Cushing's syndrome**?

A: Cortisol excess due to other illness without involvement of pituitary adrenal axis is called Pseudo-Cushing's syndrome. There is increased urinary excretion of steroid, absent diurnal variation of cortisol and failure of suppression by dexamethasone.

- It may occur in chronic alcoholism, severe depression and in simple obesity. All the features of Cushing's syndrome revert to normal after removal of the cause (features in favour of Cushing's syndrome are bruise, myopathy and hypertension, all of which are usually absent in Pseudo-Cushing's syndrome).
- To differentiate from Cushing's syndrome: Insulin-induced hypoglycaemia is helpful. In Cushing's syndrome, there is almost no response. But in Pseudo-Cushing's syndrome, there is excess cortisol secretion.

N.B. Remember; if there is history of alcohol intake, advice the patient to stop taking alcohol. Repeat cortisol or dexamethasone suppression test. It may be normal. Then further test is not recommended.

Q: How to **differentiate clinically** different types of Cushing's syndrome?

A: By history, physical examination and investigation:

1. In Cushing's syndrome due to adrenal cause:
 - In adrenal adenoma: Clinical features of glucocorticoid excess are present, but androgenic effect like hirsutism and virilization are absent and there is no pigmentation. Serum ACTH is absent or low.
 - In adrenal carcinoma: Clinical features of glucocorticoid excess are present, androgenic effects like hirsutism and virilization are rapidly progressive. Serum ACTH is absent or low.
2. In ectopic ACTH syndrome: Usually there is short history, excess pigmentation due to high ACTH level, weight loss (rather than obesity) and severe hypokalaemic alkalosis. Hypertension and oedema are more common. Classical features of Cushing's syndrome are usually absent. Serum ACTH is high.

3. In Cushing's disease: With classic features of Cushing's syndrome, there may be visual disturbance and features of hypopituitarism, also features of raised intracranial pressure like headache due to pituitary tumour. Serum ACTH level is high.
4. History of alcoholism and depression or simple obesity suggests pseudo-Cushing's syndrome.

Q: What are the causes of death in Cushing's syndrome?

A: As follows:

- Hypertension.
- Myocardial infarction.
- Heart failure.
- Infections.

Q: How to investigate Cushing's syndrome?

A: First to confirm the diagnosis and then further tests to find out the cause.

Tests to confirm Cushing's syndrome. Screening test:

- 24 hours urinary free cortisol measurement.
- Or, Overnight dexamethasone suppression test (see below).
- Or, low dose dexamethasone suppression test (see below).
- Or, late night salivary cortisol.
- Or, circadian rhythm (see below).

If normal, Cushing's syndrome is unlikely.

If anyone is abnormal, perform other tests and repeat the abnormal result.

Cushing's syndrome is confirmed by using 2 of 3 main tests:

- Failure to suppress serum cortisol with low doses of oral dexamethasone.
- Loss of normal circadian rhythm of cortisol, with inappropriately elevated late night serum or salivary cortisol.
- Increased 24-hour urine free cortisol.

If Cushing's syndrome is confirmed, other tests are done to find out the cause (to localize the site of lesion):

1. Serum ACTH:
 - If ACTH is low or undetectable: adrenal cause is likely. Then USG, CT or MRI to find adrenal lesion (tumour or hyperplasia). If no mass is seen, then adrenal vein sampling or adrenal scintigraphy should be done.
 - If ACTH is high: Likely cause in pituitary (Cushing's disease) or ectopic ACTH syndrome
2. If Cushing disease is suspected: CT or MRI of skull. MRI will show pituitary microadenoma in 70% cases. If present (usually found if >6 mm), then—
 - Corticotropin releasing hormone (CRH) test: 100 µg bovine CRHIV is given. Measure serum ACTH and cortisol for 2 hours. It increases in Cushing disease (ACTH >50%, cortisol >20%), but no response in ectopic ACTH.
 - Then—High dose dexamethasone suppression test (HDDST, see below).

3. If no pituitary mass is seen, or CRH test negative or HDDST shows <50% suppression,
 - Then—Selective catheterization of inferior petrosal sinus to measure ACTH for pituitary lesion.
 - If negative, then likely cause is ectopic ACTH syndrome.
 - Then—Chest X-ray, CT scan of chest (to see carcinoma of bronchus or bronchial carcinoid), CT scan of abdomen.

Other tests (to see the effect):

- Electrolytes (hypokalaemia).
- Blood sugar.
- Bone mass density to see osteoporosis.

Q: What are the different **dexamethasone suppression tests**?

A: As follows:

1. **Overnight dexamethasone suppression test (ONDST):** 1 mg dexamethasone orally at 11 p.m. Blood sample is taken at 9 a.m. in the next morning to measure serum cortisol.
 - Normally, almost total suppression of cortisol (<100 nmol/L).
 - Failure of suppression indicates Cushing's syndrome due to any cause.
 - This test is simple, can be done as an outpatient screening test, but may give some false positive results.
2. **Low dose dexamethasone suppression test (LDDST):** 0.5 mg 6 hourly for 2 days. Measure serum cortisol at 9 a.m. on days 0 and 2.
 - Failure of suppression of cortisol (<60 nmol/L on 2nd sample) indicates Cushing's syndrome due to any cause.
3. **High dose dexamethasone suppression test (HDDST):** 2 mg 6 hourly for 2 days. Plasma cortisol is measured at 9 a.m. on days 0 and 2.
 - Plasma cortisol on day 2 <50% of that in day 0 suggests Cushing's disease (in 90% cases).
 - Failure of suppression occurs in ectopic ACTH.
 - Or, urine cortisol <50% of basal suggests Cushing's disease and >50% of basal suggests ectopic ACTH syndrome.

Q: Why **dexamethasone** is used in suppression test? Why **not** other steroids like prednisolone?

A: Because dexamethasone does not cross react in radioimmunoassay for cortisol. But other steroids can cross react.

N.B. Remember the following points:

- Plasma cortisol levels are highly variable. So, random measurement of daytime plasma cortisol level is of no value.
- In pituitary tumour, there is high ACTH and high cortisol.
- In ectopic ACTH syndrome, there is high ACTH and high cortisol.
- In adrenal tumour, there is low or undetectable ACTH and high cortisol.
- Cushing disease and cortisol secreting adrenal tumour are 4 times common in women than men. But ectopic ACTH syndrome is more in men.

Q: What is circadian rhythm?

A: After 48 hours in hospital, cortisol samples are taken at 9 a.m. and 12 a.m. midnight (without waking the patient and ideally when asleep). Normally, serum cortisol is high in morning and low in midnight (called circadian rhythm). Patient with Cushing's syndrome has high midnight cortisol levels (>100 nmol/L), though 9 a.m. value may be normal.

Q: How to treat Cushing's syndrome?

A: It depends on the cause.

1. Cushing's disease:

- Transphenoidal removal of microadenoma.
- If surgery is not possible or unsuccessful, bilateral adrenalectomy should be done. Later, the patient may develop Nelson's syndrome (see below).
- If surgery is not possible, sometimes only external pituitary irradiation may be given. It is slowly effective in 50 to 60% cases, response in children is better than adults, 80% may be cured.
- To reduce ACTH production: Bromocriptine or cyproheptadine is rarely effective.
- Drugs such as metyrapone and ketoconazole may be given.

2. Adrenal tumour:

- In adrenal adenoma or carcinoma: surgical resection (adrenalectomy).
- In carcinoma, recurrence may occur. Radiotherapy or chemotherapy or adrenolytic drugs (mitotane) may be given.
- Other drugs: Metyrapone or ketoconazole may be used (which inhibits biosynthesis of cortisol).

3. Ectopic ACTH:

- If possible: surgical resection of primary lesion (like bronchial carcinoma or carcinoid).
- If surgery is not possible: radiotherapy or chemotherapy should be considered. Bilateral adrenalectomy may be done.

Q: What is Nelson's syndrome?

A: Nelson syndrome is characterized by increased pigmentation due to excess ACTH associated with enlarging pituitary tumour, which occurs after bilateral adrenalectomy for Cushing's syndrome.

It occurs in about 20% cases. The tumour is locally invasive. It can be prevented by pituitary radiotherapy soon after adrenalectomy.

Treatment:

- Surgical removal of the tumour of pituitary.
- Occasionally radiotherapy may be given (if it was not given previously).



Nelson's syndrome [Bilateral adrenalectomy scar (arrow below), striae, pigmentation (arrow above)]

ADDISON'S DISEASE

Instruction by the examiner:

- Perform the general examination (emaciation and pigmentation).
- Examine the patient (pigmentation). What else do you want to see?

Proceed as follows:

1. Look for pigmentation (dull, slate coloured or grey-brown) in the following sites:
 - See the whole body (may be generalized pigmentation).
 - Face and neck (exposed parts).
 - Mucous membrane of mouth (opposite the molar), lips and conjunctiva.
 - Skin crease (palmar crease), knuckles and nipples.
 - Pressure points (elbow and knee).
 - Recent scar.
2. Check for vitiligo.
3. Monitor BP: Both standing and lying (BP is low and there may be postural hypotension).
4. The patient looks emaciated.

Presentation of a Case:

- The patient has generalized pigmentation, more marked in face, neck, mucous membrane of mouth, palmar crease, knuckles, knee and elbow.
- There is also vitiligo (mention the site).
- The patient looks emaciated, BP is low and there is also postural hypotension.

My diagnosis is **Addison's disease**.

Q: What are the **causes** of pigmentation?

A: See in the chapter 'General Examination'.

Q: Mention **one investigation** in this patient to diagnose Addison's disease.

A: Serum cortisol and ACTH level.

Q: What do you **expect** in Addison's disease?

A: Low cortisol and high ACTH.

Q: What **investigation** will you do after this finding?

A: Short synacthen test (see below).

Q: What is **Addison's disease**?

A: It is the primary adrenocortical insufficiency resulting in glucocorticoid and mineralocorticoid insufficiency. There is destruction of entire adrenal cortex.

Q: What is the **size of heart** in Addison's disease?

A: Small heart.



Pigmentation in crease



Generalized pigmentation



Pigmentation in lips and gum



Pigmentation in palate

Q: What are the features or diagnostic criteria in Addison's disease?

A: Triad of:

- Weakness or emaciation (100% cases).
- Pigmentation (90% cases).
- Hypotension (88% cases). Postural hypotension is common.

(Other features: Gastroenteritis in 56%, postural symptoms 12%, salt craving 19%).

Q: What are the causes of Addison's disease?

A: As follows:

1. Common causes:

- Autoimmune: 80% (more in female).
- TB of adrenal gland: 10%.

2. Other causes (less common or rare):

- Amyloidosis.
- Sarcoidosis.
- Haemochromatosis.
- Bilateral adrenal haemorrhage: after meningococcal septicaemia (Waterhouse–Fridrichsen syndrome) and trauma.
- Lymphoma.
- Secondary deposit in adrenals.
- HIV infection.
- Bilateral adrenalectomy.

Q: Why postural hypotension in Addison's disease?

A: It is due to hypovolaemia and sodium loss. Mineralocorticoid deficiency is responsible for hypotension.

Q: What are the diseases associated with Addison's disease?

A: It is an autoimmune disease, may be associated with other autoimmune diseases, such as Graves' disease, Hashimoto's thyroiditis, pernicious anaemia, primary ovarian failure, myasthenia gravis, type-1 DM.

Q: What are the presentations of Addison's disease?

A: As follows:

- Chronic adrenocortical insufficiency (weakness, pigmentation, hypotension).
- Addisonian crisis.

Q: Why **vitiligo** in Addison's disease?

A: It is due to autoimmunity. Vitiligo is present in 10 to 20% cases.

Q: Why **pigmentation** in Addison's disease?

A: Due to excess ACTH that stimulates excess melanin production.

Q: What are the **sites of pigmentation** in Addison's disease?

A: May be generalized. Exposed parts (face, neck), skin crease (palm), knuckles, pressure points (elbow, knee), recent scar.

Q: What **investigations** should be done to diagnose Addison's disease?

A: As follows:

1. Routine tests:

- CBC (shows high eosinophil, lymphocyte and ESR). Anaemia may be present, associated with pernicious anaemia.
- Blood glucose (low or lower limit, especially during Addisonian crisis).
- Electrolytes (Hyponatraemia and hyperkalaemia. Hyponatraemia is more important than hyperkalaemia. Mild acidosis may be present.)
- Other tests: Serum renin (increases), aldosterone (low) and serum calcium (may be high).

2. Test to confirm:

- Plasma ACTH and cortisol measurement is confirmatory (high ACTH, >80 ng/L and low or lower normal cortisol).
- Short synacthen test may be done. If cortisol level rises, it rules out Addison's disease. If cortisol does not rise, it may be due to secondary adrenocortical deficiency (deficiency of ACTH), or prolonged steroid use. Then, long synacthen test can be done (however, this test is not done, because of availability of accurate ACTH assay).

3. Tests to find out causes:

- Chest X-ray (to diagnose tuberculosis).
- Plain X-ray abdomen (to see adrenal calcification in TB).
- Adrenal autoantibody (antibody to 21 hydroxylase, antibody to 17 hydroxylase).
- USG or CT scan of adrenals (to look for calcification in TB or malignancy).

4. Other tests:

- Screening for pernicious anaemia and other autoimmune disorders.
- Thyroid screening.
- Other tests according to suspicion of cause (e.g., sarcoidosis, amyloidosis, haemochromatosis, HIV, histoplasmosis, metastatic carcinoma etc.).

Q: How to perform **synacthen** test?

A: Short synacthen test may be done during anytime of the day, but better at 9 am, non-fasting. It is usually done for:

1. Addison's disease.
2. Screening test for ACTH deficiency.

Procedure:

- Short synacthen test: 250 µg ACTH (synacthen or tetracosactrin) IM or IV is given. Serum cortisol is measured at 0 and 30 min. If cortisol rises >460 nmol/L, it rules out Addison's disease. Failure to rise may indicate secondary adrenocortical insufficiency.
- Long synacthen test: 1 mg ACTH IM daily for 3 days. Serum cortisol is measured at 0, 4, 8 and 24 hours on each day. Progressive rise of cortisol indicates secondary adrenocortical insufficiency. Failure to rise indicates Addison's disease (cortisol remains <700 nmol/L 8 hour after last injection).

N.B. Remember the following:

- *If the patient is on dexamethasone or betamethasone, it will not interfere with cortisol assay (as these do not cross-react).*
- *Random cortisol is usually low in Addison's disease, but in some cases, it may be within normal or inappropriately low in seriously ill patient. So, random cortisol measurement is of no importance. However, if random cortisol is <100 nmol/L, it is highly suggestive of Addison's disease. Also, if the serum cortisol is >460 nmol/L, it rules out Addison's disease.*
- *Single test for diagnosis of Addison's disease: Simultaneous measurement of ACTH and serum cortisol level (ACTH is high, cortisol is low).*

Q: How to treat Addison's disease?

A: As follows:

1. Replacement of hormones:
 - Glucocorticoid:
 - Hydrocortisone: 10 mg after waking up, 5 mg at 12 noon and 5 mg at 6 pm.
 - Or, if hydrocortisone is not available, prednisolone: 5 mg on waking in morning and 2.5 mg at 6 pm in afternoon.
 - Mineralocorticoid: Fludrocortisone 0.05 to 0.1 mg (50 to 300 µgm) daily.
 - Androgen: Dehydroepiandrosterone (DHEA) 50 mg/day may be given in female. It increases libido and sense of well-being, but complications like acne and hirsutism may occur.
2. Treatment of cause, e.g., antitubercular therapy in tuberculosis.

General advice to the patient:

- The patient should always carry a bracelet and steroid card, in which information regarding the diagnosis, dose of steroid and doctor's contact address.
- Good nutrition, regular meal, high carbohydrate and sufficient salt.
- The patient should keep ampoules of hydrocortisone at home. If oral therapy is impossible, the patient should take injection by himself, family members or general practitioner.
- The patient should know how to increase steroid replacement dose for intercurrent illness. During intercurrent stress (fever, cold and trauma), the dose should be doubled.

Monitoring the patient:

- Proper history regarding overall well-being.
- Measurement of BP and weight.
- Serum electrolytes.

N.B. Remember the following points during stress:

1. *Intercurrent stress (fever, cold and trauma): Double dose of steroid.*
2. *During surgery:*
 - *Minor surgery: Hydrocortisone 100 mg IM or IV premedication.*
 - *Major surgery: Hydrocortisone 100 mg IM or IV 6 hourly for 24 hours, then 50 mg 6 hourly. It should be continued until the patient is capable of taking by mouth.*
3. *If gastroenteritis: IV or IM hydrocortisone should replace oral therapy.*

Q: What are the common features absolutely found in female?

A: Loss of axillary and pubic hair (which is androgen dependent), as androgens are produced only by adrenal cortex in female. This feature is not common in male, because androgen is secreted from testes.

Q: What is Addisonian crisis?

A: It is an acute severe adrenocortical insufficiency characterized by circulatory shock with severe hypotension. It is often precipitated by intercurrent disease, surgery or infection. The patient presents with muscle cramps, nausea, vomiting, diarrhoea, acute abdomen, collapse and unconsciousness. There may be unexplained fever. Laboratory findings include hyponatraemia and hyperkalaemia, and, in some cases, hypoglycaemia and hypercalcaemia.

Q: What are the causes and treatment of Addisonian crisis?

A: As follows:

Causes:

- Sudden withdrawal of steroid (common cause, if patient is on steroid for long time).
- Stress (severe infection and operation).
- Bilateral adrenal haemorrhage (meningococcal septicaemia, injury and anticoagulant).
- Thyroxine therapy in a patient with hypopituitarism without steroid therapy.

Treatment:

- Blood is taken to measure cortisol, glucose and electrolytes.
- Three problems are present: Shortage of salt, sugar and steroid (**3S**).
- IV normal saline rapidly (1 L in 30 to 60 min). Subsequently, several litres of normal saline may be required in 24 hours.
- IV 10% glucose.
- IV hydrocortisone 100 mg stat. Then hydrocortisone 100 mg IM or IV, 6 hourly, which is continued until the patient is stable and can take by mouth. Then oral steroid is started. Initially hydrocortisone 20 mg 8 hourly, reducing to 20 to 30 mg in divided doses for few days (then original replacement therapy should be given).
- Treatment of underlying cause (e.g., infection, adrenal or pituitary pathology etc.).

N.B. Remember the following:

- *In severe hyponatraemia (<125 mmol/L), hypertonic saline is unnecessary. Plasma Na should not be increased >10 mmol/L/day. This may cause central pontine myelinolysis (osmotic demyelination syndrome).*

- During crisis or acute illness, mineralocorticoid such as fludrocortisone is unnecessary, as high dose of steroid provides sufficient mineralocorticoid activity. It can be started later on.
- For hyperkalaemia, volume replacement is sufficient. No extra treatment is usually necessary, but occasionally requires specific therapy.

Q: What **drug** is avoided in acute abdominal pain in Addison's disease?

A: Morphine, as patients are more sensitive to this drug.

Q: How to **differentiate** between primary and secondary adrenocortical insufficiency?

A: As follows:

Points	Primary	Secondary
1. Site	Primary involvement of adrenal gland	Cause in pituitary or prolonged use of steroid
2. Pigmentation	Present	Usually pallor
3. BP	Low	Normal, because aldosterone secretion is not dependent on ACTH
4. Secondary sex character	Normal	Early loss of secondary sex characters. Also, there are features of deficiency of other pituitary hormones.
5. ACTH	High	Low
6. Electrolytes	Low Na ⁺ , high K ⁺	Usually normal
7. Autoimmune disease	Autoimmune diseases are associated	Unlikely

TALL STATURE

Instruction by the examiner:

- Perform the general examination.
- Look at the patient (patient looks tall). What else do you want to do?

Proceed as follows:

1. **Appearance:** If tall and obese, it may be Klinefelter's syndrome. If tall, lean and thin, it may be Marfan's syndrome.
2. **If Marfan's syndrome is suspected**, then see the following points:
 - Measure the height of the patient (from crown to heel).
 - Measure the length of arm span.
 - Measure the length of upper segment (pubic symphysis to vertex) and lower segment (pubic symphysis to sole). Normally, lower segment is larger than the upper segment (the ratio is 0.8:1).
 - Also look for arachnodactyly, high arched palate, eyes (lens dislocation) and heart (aortic regurgitation).
3. **If Klinefelter's syndrome is suspected**, then see the following points:
 - Gynaecomastia.
 - Testis (small).
 - Secondary sexual characters (small genitalia, absence of axillary, pubic and facial hair).
4. **If the above are excluded:**
 - Examine for evidence of thyrotoxicosis.
 - Examine for evidence of gigantism (tall and proportionately large body).
 - Look for anosmia (Kallmann's syndrome).
 - Take family history (familial tall stature and constitutional).

In the examination, usual cases of tall stature are:

- Klinefelter's syndrome.
- Marfan's syndrome.
- Sometimes, gigantism.

Q: What are the causes of tall stature?

A: As follows:

1. Constitutional.
2. Genetic (familial).
3. Marfan's syndrome.
4. Homocystinuria.
5. Chromosomal abnormalities (Klinefelter's syndrome, Kallmann's syndrome).
6. Endocrine (gigantism, thyrotoxicosis).
7. Miscellaneous:
 - Cerebral gigantism.
 - Extra Y syndrome (more Y-chromosome, taller but no excess GH).
 - In prepubertal hypogonadism due to any cause: Tall stature is common because of failure of fusion of epiphysis (but, postpubertal hypogonadism is not associated with tall stature because of fusion of epiphysis).

N.B. Commonest cause of tall stature: Constitutional, hereditary or early development.

KLINEFELTER'S SYNDROME

Instruction by the examiner:

- Look at the patient. What is your diagnosis? What else do you want to see?
- Perform general examination of this patient.

Presentation of the Case:

- The patient is tall and obese.
- There is bilateral gynaecomastia.
- Both testes are small and firm. Penis is also small and there is absence of pubic, axillary and facial hair.
- The voice is high pitched.

My diagnosis is **Klinefelter's syndrome**.

Q: What is Klinefelter's syndrome?

A: It is a chromosomal abnormality in which there is an extra X-chromosome associated with hypogonadism (due to small testis). It is characterized by:

- Tall stature (eunuchoid body proportion: Arm span is greater than height and leg is more long, lower extremity is greater than upper extremity).
- Obesity.
- Gynaecomastia.
- Absence or rudimentary external genitalia (small penis and testis: volume <5 ml).
- Absence of secondary sexual characters (axillary, pubic hair and beard).
- High pitched voice.

N.B. Remember the following points:

- *In mosaic, there may be normal puberty. Diagnosis is done during routine investigation for infertility.*
- *Carcinoma of breast may develop in 20% cases.*

Q: What are the usual presentations of Klinefelter's syndrome?

A: As follows:

- Poor sexual development.
- Infertility.
- Gynaecomastia.
- Small or undescended testis.
- Others: Decreased muscle tone, osteoporosis.

Q: What is the abnormality of testis?

A: Both testes are small and firm. There is seminiferous tubule dysgenesis. Hyalinization and fibrosis are present within the seminiferous tubules. Leydig cell function is impaired, resulting in hypogonadism. Also, there is azoospermia and high gonadotrophin.



Klinefelter's syndrome (Obesity, absence of beard, gynaecomastia, small penis and testes)



Klinefelter's syndrome (Obesity, gynaecomastia, small penis and testes)



Klinefelter's syndrome (Small genitalia)

Q: What are the features of eunuchoid body proportion?

A: Features are apparent from childhood:

- Tall stature with long leg.
- Hairless face (also sparse body hair).
- High pitched voice.
- Small and poorly developed external genitalia.
- Immature personality.

Q: Why patient is tall in Klinefelter's syndrome?

A: Androgen deficiency with lack of epiphyseal closure in puberty.

Q: Why gynaecomastia in Klinefelter's syndrome?

A: Due to increased oestradiol levels and increased oestradiol testosterone ratio. It is present in 30 to 50% cases.

Q: Why there is absence of secondary sexual characteristics?

A: Due to decreased androgen production.

Q: What investigations do you suggest in Klinefelter's syndrome?

A: As follows:

- Serum testosterone (low), gonadotrophic hormones (increased FSH and LH).
- Serum oestrogen (increases).
- Azoospermia is universal.
- Chromosomal analysis (two or more X-chromosome, one or more Y-chromosome).

Q: What is the common karyotype abnormality?

A: As follows:

- Usually, 47 XXY (in 80 to 90%), which results from non-dysjunction during meiosis in one of the parents.
- May be 46 XY or 47 XXY mosaic (in 10%).
- Others (rare) are, 48 XXYY, 48 XXXY, 49 XXXYY, 49 XXXXY.

Q: What are the **associations or increased incidence** in Klinefelter's syndrome?

A: The usual associations are:

- DM type-2.
- Low T₄.
- Bronchial asthma.
- Carcinoma of breast in male is more in Klinefelter's syndrome.
- Mitral valve prolapse (found in 55% cases).
- Hashimoto's thyroiditis.
- Connective tissue disease: SLE, rheumatoid arthritis, Sjögren's syndrome.

Q: How to **treat** Klinefelter's syndrome?

A: As follows:

- No specific treatment.
- Androgen (testosterone may be used in oral, injection, patch, gel and pellet).
- Plastic surgery for gynaecomastia.
- Life span is usually normal.

Cause of primary hypogonadism: It is due to defect in gonad or testes.

- Infection in testes (mumps orchitis, tuberculosis).
- Orchidectomy (before puberty).
- Cryptorchidism (undescended testes, bilateral).
- Klinefelter's syndrome.
- Noonan's syndrome.
- Myotonic dystrophy.
- Radiation to the testis.
- Haemochromatosis.

SHORT STATURE

Instruction by the examiner:

- This patient is 25 years old. Look at the patient. What is your diagnosis? What else do you want to see?
- Perform the general examination of this patient, who is 28 years old.

Proceed as follows:

1. History to be taken:

- Family history (of both parents and other family members).
- Pregnancy record (growth retardation, weight at birth and any congenital disease).
- Rate of growth.
- Systemic disease (such as respiratory, cardiac, GIT and renal).
- Nutrition (less intake of food and malabsorption).
- Age of appearance of secondary sexual characters.
- Use of steroid during childhood (if any).
- Psychosocial deprivation.

2. Physical examination:

- Height and weight chart (if height is below third percentile, it is considered as short stature).
- Arm span and height (in achondroplasia).
- Short limbs compared to trunk (in achondroplasia).
- Reduction of weight and height (in malnutrition and systemic disease).
- More weight but short height indicates endocrine disease (in hypothyroidism, Cushing's syndrome) and genetic syndrome (such as Prader–Willi syndrome, Bardet–Biedl syndrome).
- Look for evidence of systemic disease (such as heart, kidney and respiratory).
- Others (Turner's syndrome, Noonan's syndrome and pseudohypoparathyroidism).



20-year-old girl
with JIA



Pseudohypoparathyroidism



Achondroplasia



Constitutional short stature

Q: How to investigate short stature?**A:** After exclusion of systemic disease, following investigations should be done:

1. Thyroid function tests.
 - FT₃, FT₄, TSH.
 - If needed—USG of neck, radioiodine uptake test, thyroid scan etc.
2. GH status (better do the stimulation test):
 - GH response to insulin is the gold standard.
 - Serum insulin like growth factor-1 (IGF-1) and insulin like growth factor binding protein-3 (IGF-BP3).
 - Basal GH level (little value).
 - Urinary GH level (may be used as screening).
3. Bone age—non dominant hand and wrist X-ray for the assessment of bone age by comparison with standard chart (helpful for diagnosis of constitutional delay, hypothyroidism and GH deficiency).
4. X-ray skull (may show calcification in craniopharyngioma).
5. Karyotyping in female (to exclude Turner's syndrome).
6. Other tests according to the suspicion of causes.

Causes of short stature:

1. Constitutional (commonest cause).
2. Familial or genetic.
3. Physiological growth delay.
4. Emotional deprivation and psychological factors.
5. Chronic systemic disease:
 - Cardiac—congenital cyanotic heart disease (Fallot's tetralogy).
 - Renal—renal failure, renal tubular acidosis.
 - Respiratory—bronchiectasis, bronchial asthma.
 - GIT—small bowel disease (Coeliac disease), Hirschsprung's disease.
 - Others: α -Thalassaemia major, cystic fibrosis, juvenile idiopathic arthritis (JIA).
6. Endocrine diseases:
 - Hypopituitarism (pituitary dwarfism).
 - Isolated GH deficiency.
 - Cretinism (hypothyroidism).
 - Cushing's syndrome.
 - Pseudohypoparathyroidism (characterized by short stature, round face, mental retardation, epileptic attack, basal ganglia and subcutaneous calcification, short metacarpal. Hypoparathyroidism is due to defect in end organ resistance to parathormone).
 - Pseudo-pseudohypoparathyroidism.
 - Uncontrolled Juvenile diabetes mellitus.
7. Nutritional:
 - Protein energy malnutrition (marasmus and kwashiorkor).
 - Ricket.

8. Chromosomal or genetic abnormalities:

- Down's syndrome.
- Turner's syndrome.
- Noonan's syndrome (male Turner).
- Prader–Willi syndrome.
- Bardet–Biedl syndrome.

9. Skeletal dysplasia:

- If there is short limb and normal trunk, may be due to achondroplasia.
- If there is short limb and short spine, may be due to mucopolysaccharidoses (Hurler's syndrome or Gargoylism).

10. Gross kyphoscoliosis.**11. Drugs like steroid.**

ACHONDROPLASIA

It is a genetic disorder, inherited as autosomal dominant, characterized by disproportionately short arms and legs. Features are:

- Short stature.
- Large head with prominent forehead. Face is small, nasal bridge is flat.
- Short and broad limbs (both upper and lower).
- Trunk has normal growth.
- Normal development: Dental, endocrine, sexual.
- Normal intelligence.

It results from defect in the fibroblast growth factor receptor-3 gene. There is decrease in proliferation of the cartilage present in growth plate.

Q: What is dwarfism?

A: It is defined as short stature in which height of a person is much below than the normal, according to the chronological age.

DIABETES MELLITUS

Short cases in any clinical examination related to DM are already described in Chapter 1. Usual cases are:

- Diabetic foot (page 80)
- Leg ulcer (page 74)
- Diabetic amyotrophy (page 85)
- Lipodystrophy of thigh (page 87)
- Necrobiosis lipoidica diabetorum (page 88)
- Diabetic neuropathy (page 580)
- Diabetic retinopathy (page 864).

In a diabetic patient, examination involves multiple systems of the body. General inspection may give a clue to any underlying cause as DM. Look at the face (e.g., Cushing's syndrome and acromegaly, which are the causes of secondary DM). Generalized pigmentation occurs in haemochromatosis called bronze diabetes. In general examination findings of any complication may be found (e.g., diabetic foot, nephropathy, neuropathy etc.).

Instruction by the Examiner (Case No. 1):

- Perform the general examination of this diabetic patient.

Proceed as follows:

1. Look at the patient to see:
 - Cachexia (in type-1 DM) or obesity (in type-2 DM).
 - Generalized pigmentation (found in haemochromatosis called bronze diabetes).
 - Kussmaul's breathing or air hunger (found in diabetic ketoacidosis).
2. Look at the face:
 - Signs of Cushing's syndrome, thyrotoxicosis or acromegaly (which may cause DM).
 - Xanthelasma, corneal arcus, ocular palsy and other obvious cranial nerve palsy (e.g., Bell's palsy).
3. Examine the oral cavity for oral candidiasis.
4. Examine the neck for thyromegaly (DM may occur in thyrotoxicosis).
5. Examine the neck and axilla for acanthosis nigricans (associated with insulin resistance).
6. Look for dehydration (in diabetic ketoacidosis) and sweating (in hypoglycaemia) or oedema (diabetic nephropathy).
7. Examine the skin for hypopigmentation (vitiligo may indicate autoimmune cause of DM), diabetic dermopathy, ulcer, infections (boils, carbuncle, cellulitis), necrobiosis lipoidica diabetorum, fat atrophy or hypertrophy at injection sites, granuloma annulare, hair loss and skin atrophy. Look for fungal infection in nails.
8. Look for any obvious muscle wasting (in thigh called diabetic amyotrophy) or joint deformity (Charcot's joint) and Dupuytren's contracture or trigger finger. Also in lower limbs, look for calluses, nail change, ankle reflex and foot deformities such as hammer or claw toes.
9. Feel the peripheral pulses (reduced or absent in atherosclerosis), look for fixed heart rate or loss of sinus dysrhythmia (autonomic neuropathy) and auscultate carotid arteries (for bruit in atherosclerosis).

10. BP (lying and standing to see postural hypotension, found in autonomic neuropathy).
11. At the end, examine the urine for sugar, proteinuria and ketone bodies.

Instruction By the Examiner (Case No. 2):

- Examine the lower or upper limbs of this Diabetic patient.

Proceed as follows (lower limbs):

1. Inspection:
 - Necrobiosis lipoidica diabetorum (central yellow scar with surrounding red margin, found over the shins, due to atrophy of subcutaneous collagen).
 - Ulceration and infection (boils, abscess, gangrene, carbuncle and cellulitis). Look at the sole and between the toes.
 - Diabetic dermopathy (small rounded plaques with raised border over the shins in a linear fashion). Look for any pigmented scars (late diabetic dermopathy).
 - Injection marks on thighs and fat atrophy or hypertrophy.
 - Hair loss and skin atrophy (found in small vessel disease).
 - Muscle wasting (due to neuropathy or diabetic amyotrophy or as a part of generalized wasting).
 - Examine both knee joints (swollen joints and deformity indicates Charcot's joints).
2. Palpation:
 - Temperature (may be cold and blue due to peripheral vascular disease and associated skin atrophy or absent pulses).
 - Pulsation (absent due to peripheral vascular disease or atherosclerosis) and bounding pulse (in neuropathy).
 - Pitting oedema (nephropathy and autonomic neuropathy).
3. Auscultate over femoral artery (for bruit).
4. Perform neurological examination of lower limbs to see peripheral neuropathy (see in chapter 'Neurology' page 648).

Instruction By the Examiner (Case No. 3):

Examine eyes of this Diabetic patient.

Proceed as follows:

- Look for xanthelasma and corneal arcus (occurs in hyperlipidaemia in association with DM).
- Acuity of vision.
- Argyll Robertson pupil.
- Rubeosis iridis (new vessels on the anterior surface of iris).
- Cataract.
- Examine the cranial nerves III, IV and VI (especially 3rd nerve palsy. If occurs in DM, it spares the pupil).
- Finally, perform fundoscopic examination for diabetic retinopathy.

Q: What **investigations** do you suggest in this case?

A: As follows:

- Urine R/M/E.
- Blood sugar (fasting and 2 hour after breakfast).
- HbA_{1c}.
- CBC with ESR.
- Blood urea and serum creatinine.
- Serum lipid profile.
- USG of whole abdomen.
- CXR PA view.
- Plain X-ray abdomen to see pancreatic calcification.
- ECG.

Q: What are the causes of **loss of vision** in DM?

A: As follows:

- Diabetic retinopathy.
- Cataract.
- Age related macular degeneration.
- Retinal vein occlusion.
- Retinal artery occlusion.
- Non-arteritic ischaemic optic neuropathy.
- Glaucoma.

READ THE FOLLOWING TOPICS IN RELATION TO DIABETES MELLITUS

Q: What are the **criteria** for the diagnosis of DM?

A: Criteria for diagnosis of DM are:

In symptomatic patients, diagnoses is made by (any 1 of the following):

- Fasting plasma venous blood sugar level ≥ 7.0 mmol/L.
- Random glucose or 2 hours after 75 g glucose, blood sugar is ≥ 11.1 mmol/L.

In asymptomatic patients, 2 diagnostic tests are required to confirm diabetes.

- HbA_{1c} > 6.5 (48 mmol/mol). HbA_{1c} can be used as a diagnostic test for diabetes.

N.B. Remember the following points:

- *Random means without regard to time since the last meal.*
- *Fasting means no calorie intake for 8 hours at least (not more than 16 hours).*
- *Fasting blood sugar < 5.6 mmol/L is normal.*
- *In symptomatic patient: 1 abnormal finding is diagnostic of DM (as above).*
- *In asymptomatic patients: 2 values are required (as above).*
- *For OGTT, only fasting glucose and 2 hours after 75 g of glucose are sufficient for diagnosis.*
- *OGTT should be done only for borderline cases (fasting glucose 6.1 to 7.0 mmol/L or random glucose 7.8 to 11.0 mmol/L) and also for the diagnosis of gestational diabetes mellitus (GDM).*

Q: What is impaired glucose tolerance (IGT)?

A: When fasting glucose is <7 mmol but during OGTT, 2 hours after 75 gm glucose is 7.8 to 11.0 mmol, it is called IGT. The patient who has IGT is at increased risk of developing frank DM type-2 with time and also macrovascular complications are more (mainly cardiovascular).

Lifestyle modification for type-2 DM and annual check-up for glucose are recommended for this patient. Cardiovascular risk factors should be treated aggressively.

Q: What is impaired fasting glucose (IFG)?

A: IFG is defined as the fasting glucose level between 6.1 and 6.9 mmol/L (110 to 125 mg/dL) and 2 hours after 75 gm glucose is <7.8 (<140 mg/dL) according to WHO. However, American Diabetes Association (ADA) defines it as fasting glucose level between 5.6 and 6.9 mmol/L (100 to 125 mg/dL). These patients are prone to develop frank DM and cardiovascular disease. The patient is advised for weight reduction of about 5 to 10% of their body weight, regular exercise and follow-up. Usually no drug therapy is recommended.

*N.B. Patients with IGT and/or IFG are now regarded as **pre-diabetics**.*

Q: What is latent diabetes?

A: It means blood glucose is usually normal, but may be high under certain stressful conditions (such as pregnancy, infection, obesity, stress or drugs like steroid, thiazide diuretics).

Q: What is potential Diabetes?

A: It means blood sugar usually is normal, but the patient has increased risk of developing DM in future due to genetic reasons like:

- Both parents are diabetic.
- One parent is diabetic and the other has a family history of diabetes.
- Has a diabetic sibling.
- In a twin, if one is diabetic.

Q: What is brittle diabetes?

A: Brittle diabetes (or unstable diabetes or labile diabetes) refers to uncontrolled insulin-dependent DM with recurrent, dramatic, large swings in blood glucose levels, often without any apparent reason. This leads to irregular and unpredictable hyperglycaemia, frequently with ketosis and sometimes serious hypoglycaemia.

Brittle diabetes occurs in 1 to 2% of diabetics, usually in young (15 to 30 years) patient with type-1 DM, but may also be found in elderly patient with type-1 or type-2 DM. It often develops after total pancreatectomy. It may be caused by gastrointestinal absorption problems including delayed stomach emptying (gastroparesis), drug interactions, problems with insulin absorption or hormonal malfunction.

Q: Classify DM aetiologically.

A: Aetiological classification of DM:

1. Type-1 DM:
 - Idiopathic.
 - Immune mediated.
2. Type-2 DM.
3. Gestational DM.

4. Other specific types:

- Genetic defects of β -cell function.
- Genetic defects of insulin action.
- Genetic syndromes such as Down's syndrome, Klinefelter's syndrome, Turner's syndrome and DIDMOAD (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness) syndrome.
- Pancreatic diseases (such as chronic pancreatitis and haemochromatosis).
- Endocrine diseases (such as acromegaly, Cushing's syndrome, glucagonoma and thyrotoxicosis).
- Drug induced (e.g., corticosteroid).
- Viral infections (e.g., congenital rubella, mumps, Coxsackie virus B).
- Uncommon form of immune-mediated DM.

Q: What is insulin resistance syndrome or metabolic syndrome or syndrome X?

A: Type-2 DM associated with central obesity, hypertension, dyslipidaemia (elevated LDL and triglyceride, but low HDL), non alcoholic fatty liver disease, PCOS (in female) is called metabolic syndrome or insulin resistance syndrome. Other features are hyperinsulinaemia, microalbuminuria, elevated fibrinogen and plasminogen activator inhibitor 1, plasma uric acid and increased sympathetic activity. The primary defect is insulin resistance. This predisposes to increased risk of cardiovascular disease.

Q: What are the complications of DM?

A: As follows:

1. Acute complications:

- Hypoglycaemia.
- Diabetic ketoacidosis.
- Hyperglycaemic hyperosmolar state (previously called hyperosmolar non-ketotic diabetic coma).
- Lactic acidosis.

2. Long term or late complications:

A. Microvascular:

- Neuropathy: Peripheral neuropathy (sensory, motor or mixed), mononeuritis multiplex, mononeuropathy, autonomic neuropathy.
- Nephropathy (CKD).
- Eye complications (retinopathy, cataract).
- Foot complications (ulcers, gangrene, arthropathy).

B. Macrovascular:

- Coronary circulation: Myocardial ischaemia, infarction.
- Cerebral circulation: Transient ischaemic attack (TIA), cerebrovascular diseases (CVD).
- Peripheral circulation: Ischaemia, claudication.
- Foot complications (ulcers, gangrene, arthropathy).

C. Others: Abscess, boil, carbuncle, cellulitis, tuberculosis.

N.B. DM can cause painless or silent myocardial infarction. Foot complications are due to both macro and microvascular.

Q: What are the types of neuropathy in DM?**A:** As follows:

- Sensory neuropathy (common).
- Mixed motor and sensory neuropathy.
- Asymmetrical motor neuropathy (diabetic amyotrophy).
- Autonomic neuropathy.
- Mononeuropathy.
- Mononeuritis multiplex.

Mechanism of neuropathy in DM:

- Axonal degeneration.
- Patchy or segmental demyelination.
- Involvement of intraneural capillaries.

Q: What are the features of autonomic neuropathy in DM?**A:** In both type-1 and type-2 DM, there may be autonomic neuropathy, which involves multiple systems of the body. Features are:

- CVS: Postural hypotension, fixed heart rate, resting tachycardia, sometimes sudden death.
- GIT: Gastroparesis, nocturnal diarrhoea, constipation.
- Genitourinary: Urinary incontinence, difficulty in micturition, erectile dysfunction and retrograde ejaculation.
- Sudomotor: Gustatory sweating, nocturnal sweating without hypoglycaemia, hyperhidrosis of upper extremity and anhidrosis of lower extremity, anhidrosis of foot can cause cracked skin and ulcer.
- Vasomotor: Cold feet due to loss of vasomotor response, dependent oedema due to loss of vasomotor tone and increased vascular permeability.
- Autonomic neuropathy can reduce counter-regulatory hormone release, leading to inability to sense hypoglycaemia.
- Pupillary: Decreased pupil size, resistance to mydriatic drugs, delayed or no reflex to light (called pseudo-Argyll Robertson pupil).

Q: What are the causes of painless myocardial infarction?**A:** As follows:

- DM with autonomic neuropathy.
- Elderly patient with dementia.
- CVD.

Q: What are the causes of sudden death in DM?**A:** It is more likely due to autonomic neuropathy. Patient usually dies from sudden cardio-respiratory arrest.**Q: What are the commonest cause of hypoglycaemia?****A:** As follows:

- Excess dose of drug or insulin.
- Missed meal after insulin or oral hypoglycaemic agent.
- Severe exercise.
- Factitious (deliberately induced).
- Alcohol.

Q: What are the **differences** between hypoglycaemic coma and diabetic coma (coma with ketoacidosis)?

A: As follows:

Points	Hypoglycaemic Coma	Diabetic Coma (DKA)
1. History	Excess insulin, but no or insufficient food intake, heavy exercise	Too little or no insulin but there may be concurrent infection or digestive disturbance
2. Onset	Rapid onset, usually after taking insulin. Patient is in good health prior to this	Slow onset, patient has ill health for several days
3. Symptoms	Weakness, tremor, sweating, palpitation, hunger, occasional vomiting from depot insulin	Excessive thirst, polyuria, dehydration, vomiting, air hunger, abdominal pain
4. Signs		
• Skin and tongue	Moist	Dry
• Eyes	Normal	Sunken
• Pulse	High volume, tachycardia	Weak
• BP	Normal or raised	Low
• Breathing	Shallow or normal	Kussmaul's breathing
• Acetone smell	Absent	Present
• Reflexes	Brisk	Diminished
• Plantar response	Often extensor	Usually flexor
5. Urine		
• Ketone body	Absent	Present
• Glycosuria	Absent	Present
6. Blood		
• Glucose	Hypoglycaemia	Hyperglycaemia
• Bicarbonate	Normal	Reduced
• pH	Normal	Low (metabolic acidosis)
• Acetone	Normal	High
7. Treatment	Oral or IV glucose	Insulin and others
8. Prognosis	Good	Bad

Q: How to diagnose clinically a case of **hypoglycaemia** and **hyperglycaemic coma**?

A: Typical features of hypoglycaemic are:

Autonomic:

- Excessive sweating.
- Tremor.
- Palpitation (Tachycardia).
- Hunger.
- Anxiety.

Neuroglycopenic:

- Confusion.
- Drowsiness.
- Speech difficulty.
- Inability to concentrate.
- Incoordination.
- Irritability.
- Other: Jerks may be brisk, planter is bilaterally extensor.

Typical features of hyperglycaemic coma are:

- Severe dehydration.
- Pulse: Weak, BP is low.
- Air hunger is present: Kussmaul's breathing and acetone in the breath are present.
- Others: Reflexes are reduced, planter is flexor.

Q: What is **gestational diabetes mellitus (GDM)**? How is it diagnosed?

A: It is defined as any degree of glucose intolerance with the onset or first recognition during pregnancy. It constitutes 90% of women with pregnancy complicated by diabetes. More than 50% women ultimately develop diabetes in the next 20 years and this is linked with obesity. Mostly they develop type-2 DM. OGTT with 75 gm of glucose is used as a screening test for GDM for women between 24 and 28 weeks of gestation. Blood glucose is measured at fasting, 1 and 2 hour after glucose load. GDM is diagnosed if blood glucose is: Fasting ≥ 5.1 mmol/L, or after 1 hour ≥ 10 mmol/L, or after 2 hours ≥ 8.5 mmol/L.

Management of GDM:

- Dietary modification.
- Monitoring of blood glucose regularly: premeal glucose should be < 5.5 mmol/L and postmeal glucose < 7 mmol/L.
- If drug is necessary: metformin or glibenclamide is safe (does not cross placenta). Insulin may be required in later stage.
- After delivery, glucose usually becomes normal. Follow-up is necessary.
- There is risk of type 2 diabetes, 15 to 55% in 5 years. So, dietary and life style advice are necessary to reduce the risk.

Q: What are the complications of foetus in DM during pregnancy?

A: As follows:

- Teratogenicity (if DM in early pregnancy, in first 6 weeks), there may be cardiac, renal and skeletal malformations, caudal regression syndrome, neural tube defect.
- Foetal macrosomia (if DM is present in later pregnancy).
- Neonatal hypoglycaemia (as maternal glucose crosses the placenta, but insulin cannot. As a result, foetal islet cells secrete excess insulin, which may cause neonatal hypoglycaemia).
- Increased risk of polycythaemia, hyperbilirubinaemia and hypocalcaemia.
- Hyaline membrane disease.
- Stillbirth.

Q: What is the cause of macrosomia in DM?

A: Macrosomia means large or big baby (birth weight >90 percentile for gestational age). It is due to persistent maternal hyperglycaemia leading to foetal hyperglycaemia and prolonged foetal hyperinsulinism. This stimulates excessive somatic growth mediated by insulin-like growth factors (IGFs). Macrosomia affects all organs except the brain.

BRIEF NOTE ABOUT HYPERGLYCAEMIC HYPEROSMOLAR STATE (HSS)

Def: It is characterized by very high blood glucose (>30 mmol/L), high plasma osmolality (>320 mOsm/kg) and dehydration without ketoacidosis. Insulin deficiency is partial, some endogenous insulin is present, which is sufficient to inhibit hepatic ketogenesis, but insufficient to control hyperglycaemia. It may be the first presentation of diabetes mellitus, common in elderly with type 2 (NIDDM). Previously it was called hyperosmolar nonketotic diabetic coma (HNDC). There may not be coma.

Precipitating Factors: Intake of glucose rich diet, drugs (thiazide, steroid), myocardial infarction, infection (pneumonia, UTI).

Features: Polyuria, polydipsia, altered consciousness, convulsion. Signs of severe dehydration are present.

Investigations: Blood glucose (very high), plasma osmolality (>320 mOsm/kg), serum and urinary ketone body (absent), pH (normal).

Treatment:

- IV $\frac{1}{2}$ strength saline (0.45%) should be given. When osmolality is normal, 0.9% normal saline should be given. However, if hypovolaemia is present as evidenced by hypotension and oliguria, 0.9% saline may be given. Usually 4 to 6 litres fluid may be required in first 8 to 10 hours.
- Low dose soluble insulin preferably with insulin pump, 2 to 6 units hourly. Insulin dose is adjusted to reduce glucose by 50 to 70 mg/dL/hour.
- When glucose is 250 mg/dL, 5% dextrose in either aqua or 0.45% saline or 0.9% saline. Glucose infusion should be adjusted to maintain between 250 to 300 mg/dL in order to reduce the risk of cerebral oedema. When the urinary output is 50 mL/hour or more, IV fluid may be stopped.
- Other treatment: NG tube feeding, catheter if needed, antibiotic if infection, correction of electrolytes, low dose heparin (as thrombosis is common).

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NEPHROLOGY

7

MASS IN FLANK (RENAL)	589	MASS IN LEFT OR RIGHT ILIAC FOSSA	
BILATERAL RENAL MASS (POLYCYSTIC KIDNEY		(TRANSPLANTED KIDNEY)	597
DISEASE)	591	NEPHROTIC SYNDROME	601
UNILATERAL MASS (RENAL CELL			
CARCINOMA)	594		

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NEPHROLOGY

7

‘One of the first duties of the physician is to educate the masses not to take medicine’
—Sir William Osler

Short cases related to renal disease are limited. Only common problems such as, renal mass may be selected as a short case. Usual cases are:

- Bilateral renal mass (e.g., Polycystic kidney disease).
- Unilateral renal mass (e.g., renal cell carcinoma or hydronephrosis).
- Nephrotic syndrome.
- Mass in the right or left iliac fossa (e.g., transplanted kidney).

Instruction by the examiner:

- Examine the abdomen.
- Examine the abdomen and see the relevants.
- Palpate the abdomen. What are your findings?

N.B.: For details, see Chapter 4 ‘Abdomen’.

Once asked to examine the abdomen in relation to nephrology, very likely findings are:

- Unilateral renal mass (which may be due to renal cell carcinoma or hydronephrosis).
- Bilateral renal mass (which may be due to polycystic kidney disease).
- Mass in the right or left iliac fossa (transplanted kidney).
- Abdominal distension due to ascites (as in nephrotic syndrome).

Once a **renal mass or suspicion of any renal disease** is present, examiner may ask ‘What relevants do you like to see?’ Your answer should be, ‘I want to see . . .’

- General features: Pale, pigmented, puffy face with baggy eyelids (in acute glomerulonephritis, CKD), generalized oedema (in nephrotic syndrome), scratch mark for itching (in CKD).
- Skin lesion like scabies (may be related to post-streptococcal glomerulonephritis).
- Anaemia (indicates chronic kidney disease) or plethoric face (indicates secondary polycythaemia in polycystic kidney disease).
- Blood pressure (there may be previous hypertension causing CKD or, renal disease may cause hypertension as in acute glomerulonephritis, renal artery stenosis, chronic glomerulonephritis).
- Tachypnoea or breathing abnormality (Kussmaul’s breathing) in CKD.
- History of heart failure (may lead to CKD due to hypovolaemia). Auscultate for pericardial rub (indicates uraemic pericarditis).
- Arteriovenous fistula in the wrist or below the clavicle (indicates haemodialysis).

- Any features of systemic diseases that may cause renal failure (such as DM, SLE, rheumatoid arthritis, systemic sclerosis, polyarteritis nodosa, Wegener's granulomatosis).
- Fundoscopy (hypertensive retinopathy).

Examiner may ask, 'What history do you like to take related to renal disease?' Your answer should be 'I would like to take history of prolonged use of NSAID in arthritis, which may cause CKD, tubulointerstitial nephritis, analgesic nephropathy etc.' Other drugs like allopurinol, sulphonamide may also cause CKD. Also, history of DM, hypertension or any other systemic illness.

After finishing the physical examination, examiner may ask, 'Do you like to perform any bedside investigation?' Answer with 'yes, I want to perform bed side urine examination for albumin (in nephrotic syndrome) and sugar (may be related to diabetic nephropathy)'.

MASS IN FLANK (RENAL)

Instruction by the examiner:

- Examine the abdomen or, palpate the abdomen. What are your findings?

Presentation of Case (Unilateral Renal Mass): Case No. 1

- There is a mass in right (or left) loin or flank, 10×9 cm, round in shape, non-tender, surface is smooth or irregular, moves with respiration.
- Get above the swelling is present.
- On percussion, there is resonance over it (colonic resonance).

My diagnosis is **Renal mass** (mention right or left), which may be due to (causes of unilateral renal mass):

- Renal cell carcinoma (in elderly) or Wilms tumour (in children).
- Unilateral hydronephrosis or pyonephrosis.
- Hypertrophied single kidney (if nephrectomy of other kidney or congenitally one kidney is absent).
- Renal cyst (usually large).
- Polycystic kidney with single palpable kidney (due to asymmetrical enlargement).

N.B.: Right kidney may be normally palpable.

Q: Suggest one investigation.

A: Ultrasonography of whole abdomen.

Q: What investigations do you suggest?

A: As follows:

- USG of whole abdomen.
- CBC with ESR.
- Urine RME.
- Blood sugar.
- Blood urea, serum creatinine.
- Serum electrolytes.
- CT scan or MRI of renal system.
- Intravenous urography.
- Renal biopsy (USG guided) if needed.
- Other investigation according to the history and suspicion of cause.

Presentation of Case (Bilateral Renal Mass): Case No. 2

- Bilateral masses are present in both right and left flanks, right (or left) is larger, surface is irregular, margin is round or irregular, non-tender and freely movable from underlying structure.
- I can get above the swelling.
- On percussion, there is resonance over the mass.

My diagnosis is **Bilateral renal mass**, which may be due to (causes of bilateral renal mass):

- Polycystic kidney disease.
- Bilateral hydronephrosis.
- Bilateral renal cyst (usually large).
- Diabetic nephropathy in early stage.
- Amyloidosis.
- Rarely, bilateral renal cell carcinoma (occurs in von-Hippel–Lindau syndrome).

Q: What do you think the **commonest or likely cause** in this case?

A: Polycystic kidney disease.

Q: Suggest **one investigation**.

A: Ultrasonography of whole abdomen.

Q: Mention **another investigation** for your diagnosis.

A: CT scan of kidney.

Q: What **other investigations** do you suggest?

A: As above.

BILATERAL RENAL MASS (POLYCYSTIC KIDNEY DISEASE)

Instruction by the examiner:

- Examine the abdomen or, palpate the abdomen and see the relevants.

Presentation of a Case: See above (As Case No. 2).

Q: What is polycystic kidney disease (PKD)?

A: It is an inherited cystic disease of the kidney. It is 2 types:

- Adult polycystic kidney disease (APKD), inherited as autosomal dominant. It is usually common type (prevalence is approximately 1:1000). Males and females are equally affected.
- Infantile polycystic kidney disease (IPKD), inherited as autosomal recessive. It is rare and associated with hepatic fibrosis, usually fatal in the first year due to hepatic or renal failure.

Q: What are the presentations of adult PKD?

A: As follows:

1. May be asymptomatic, detected mass on routine examination or investigation (such as USG).
2. Common features are:
 - Discomfort, pain or heaviness in the loin.
 - Recurrent painless haematuria (due to rupture of cyst in renal pelvis or infection), recurrent urinary tract infection.
 - Acute loin pain or renal colic (due to haemorrhage into a cyst).
 - Features of hypertension (usually after 20 years of age).
 - Features of renal failure (in advanced stage).
 - Cerebrovascular disease (such as subarachnoid haemorrhage, due to rupture of Berry aneurysm. Or cerebral haemorrhage as a complication of hypertension).
3. Other features: polycythaemia (due to increased erythropoietin secretion), renal stone in 10% cases (associated with uric acid, which is radiolucent), renal neoplasm rarely.

Q: What are the diseases associated with PKD?

A: As follows:

- Cystic liver in 30% (common in infantile type), hepatic dysfunction is rare. Also cyst in spleen (5%), ovary and pancreas.
- Berry aneurysm in circle of Willis in 10% (may rupture causing subarachnoid haemorrhage).
- May be associated with mitral valve prolapses (25%) causing mitral regurgitation and aortic regurgitation (rarely severe).
- Mitral and aortic regurgitation (frequent but rarely severe).
- Colonic diverticula.
- Abdominal wall hernia.
- More common in sickle cell disease, cystic fibrosis, Huntington's disease.

N.B. Remember the following points:

- PKD is a misnomer, cyst occurs in many other organs (liver, spleen).
- Polycystic kidney disease is usually not premalignant.
- Hypertension is present in 75% cases.
- Usually there is polycythaemia due to high erythropoietin. There may be anaemia if CKD develops (however, haemoglobin level is higher than expected for the degree of renal failure).

Q: Can PKD be **unilateral**?

A: PKD is always bilateral (may be unilateral, if other kidney is absent either congenitally or following nephrectomy).

Q: What are the causes of **acute pain** in PKD?

A: Pain is due to:

- Acute haemorrhage in the cyst.
- Infection in the cyst.
- Renal stone.

Q: If the patient is **unconscious**, what is likely **diagnosis**?

A: Subarachnoid haemorrhage (due to rupture of berry aneurysm). Other causes may be:

- Cerebral haemorrhage as a complication of hypertension.
- Sometimes, hyponatraemia (due to salt losing nephropathy).

Q: What are the **causes of death** in PKD?

A: Death may be due to:

- Chronic kidney disease (in 1/3rd cases).
- Subarachnoid or intracerebral haemorrhage.
- Myocardial infarction.

Q: What **investigations** do you suggest?

A: As follows:

- USG (always mention the first investigation).
- Urine R/E (haematuria) and C/S.
- CBC (polycythaemia may occur).
- Renal function tests (urea, creatinine).
- Serum electrolytes (some cases are salt loser).
- High resolution CT or MRI.
- Intravenous urograms (less done nowadays, as USG is more sensitive test).

Q: What are the **findings** in IVU in polycystic kidney disease?

A: IVU shows:

- Enlargement of both kidneys.
- Elongation, stretching and distortion of pelvicalyceal system, giving rise to **spidery** appearance.

Q: How to manage the patient of PKD?

A: Usually management is symptomatic and supportive.

- Control of hypertension.
- Control of urinary tract infection.
- Plenty of fluid and also extra salt in some cases (there may be salt loser).
- Large cyst: May be aspirated under ultrasonography guidance. Or, in some case, laparoscopic cystectomy may be done.
- Treatment of renal failure (either dialysis or renal transplantation).
- Vasopressin (V_2) receptor antagonist (Tolvaptan): reduces cyst growth and slow the rate of progression of renal failure. Not widely used due to hepatotoxicity.
- Octreotide: long acting somatostatin analogue, reduces rate of growth of both liver and renal cysts.
- Genetic counselling.
- Family screening (any family member after 20 years of age, USG is done to detect cyst).
- Magnetic resonance angiography to detect berry aneurysm may be considered if any family member with PKD has history of subarachnoid haemorrhage.

Q: What are the features of infantile PKD?

A: It is rare, inherited as autosomal recessive and is associated with cyst in other organs and hepatic fibrosis. It is fatal in the first year of life, death is due to renal failure or hepatic failure.

Q: What are the cystic diseases of kidney?

A: As follows:

- Simple cyst, usually congenital.
- Acquired cyst, after dialysis (in CKD).
- Polycystic kidney disease.
- Medullary sponge kidney (unknown cause, not genetic. Cyst is confined to the papillary collecting ducts. Age 40 to 60 years, prognosis good. Usually no hypertension or no renal failure).
- Medullary cystic disease (small cyst in cortical or corticomedullary junction. Renal failure is common, hypertension may occur. The patient usually suffers from polyuria, increased thirst and salt losers).

Q: What are the causes of bilateral renal cyst or disease that mimic PKD?

A: As follows:

- Multiple simple cyst.
- Tuberous sclerosis.
- Von Hippel–Lindau syndrome.
- Multicystic dysplastic kidney.
- Juvenile nephronophthisis.
- Medullary cystic kidney disease.
- Glomerulocystic kidney disease.
- Acquired cystic disease.
- Renal cell carcinoma with cystic change.

UNILATERAL MASS (RENAL CELL CARCINOMA)

Instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case: See in Unilateral Renal Mass.

My diagnosis is **Unilateral renal mass**. For differentials, see above (mass in flank, case No. 1)

Q: What is the likely **cause** in this elderly man?

A: Renal cell carcinoma.

Q: What is renal cell carcinoma?

A: Renal cell carcinoma (or hypernephroma) is an adenocarcinoma arising from proximal tubular epithelial cells. It is usually unilateral. But in 10% cases, it may be bilateral.

Renal cell carcinoma is highly vascular. Microscopically, 85% are clear cell carcinoma (large cells with clear cytoplasm). Haemorrhage and necrosis give the cut surface a characteristic mixed golden yellow and red appearance.

In von Hippel–Lindau syndrome, inherited as autosomal dominant, there may be bilateral renal cyst, renal adenoma and renal cell carcinoma.

Q: How the patient **presents** in renal cell carcinoma?

A: Common in elderly (65 to 75 years of age), more in male. The patient may be asymptomatic in 50% cases, detected incidentally on routine investigation. May present with:

- Painless haematuria (in 60% cases).
- Loin pain or heaviness (in 40% cases).
- Palpable mass in loin (in 25 % cases).
- 10% may present with triad of painless haematuria, loin pain and loin mass (typical).

Other features:

- In 20% cases, pyrexia of unknown origin may be the only manifestation.
- Features of anaemia and hypertension.
- Malaise, anorexia, weight loss.
- In 5% cases, there may be polycythaemia.
- Features of metastasis: It may spread along the renal vein to inferior vena cava. Carcinoma of left kidney may spread along the left renal vein, which may obstruct the left testicular vein leading to left sided varicocele. Direct invasion of perinephric tissue is also common. Para-aortic lymph node may be involved (lymphatic metastasis). Blood borne metastasis to any distant organ may occur (commonly lung, bone and brain).

Q: Why **PUO** in renal cell carcinoma?

A: **Probably** due to secretion of pyrogen by tumour.

Q: If the patient has **fever with unilateral renal mass**, what other diagnosis is possible?

A: Renal tuberculosis.

Q: What investigations do you suggest?

A: As follows:

- USG of whole abdomen.
- Urine for RME (haematuria may be present).
- CBC, ESR (anaemia, may be polycythaemia).
- CT or MRI (MRI is better for tumour staging).
- IVU.
- USG or CT guided FNAC (for confirmation).
- Other investigations for metastasis, e.g., X-ray chest, liver function tests, isotope bone scan etc.

Q: What may be the haemoglobin status of this patient?

A: Usually normocytic and normochromic anaemia. Rarely, polycythaemia (in 5% cases).

Q: Why polycythaemia?

A: Due to excess erythropoietin, secreted by neoplastic cells.

Q: What peptide hormones may be produced by renal cell carcinoma?

A: Erythropoietin, renin, ADH, parathyroid hormone related peptide.

Q: If the patient has hypercalcaemia, what may be the cause?

A: Due to bony metastasis or secretion of parathormone like substance by the tumour.

Q: What electrolyte abnormality may occur?

A: Hypokalaemia.

Q: How to treat renal cell carcinoma?

A: As follows:

1. Surgery:
 - Radical nephrectomy including removal of peri-renal fascial envelope and ipsilateral para-aortic lymph nodes should be done, if possible (it should be done even if metastasis is present, as it reduces the systemic features and regresses metastasis).
 - Partial nephrectomy may be done if there are bilateral tumours or the contralateral kidney has poor functional capacity.
2. If surgery is not possible due to high operative or other risk (e.g., single functioning kidney): small tumours may be treated percutaneously by radiofrequency ablation or by tissue sparing surgery or cryoablation.
3. Medroxyprogesterone acetate may be used in metastatic disease.
4. Some benefit may be found with immunotherapy using interferon and interleukin-2.
5. New drugs are:
 - Tyrosine kinase inhibitors, e.g., sorafenib, sunitinib, pazopanib, axitinib.
 - mTOR (mammalian target of rapamycin) inhibitors, e.g., temsirolimus and everolimus.
 - Bevacizumab, an antibody against vascular endothelial growth factor (VEGF), may slow the progression in metastatic disease. Sometimes, may be used with interferon.
6. Radiotherapy has no role in RCC. However, it may be used for symptomatic relief in metastatic disease.

Prognosis: 5 year survival rate is 60 to 70%, if tumour is confined to the renal parenchyma, 15 to 35%, if there is lymph node involvement and 5%, if there is distant metastasis.

BRIEF NOTES ON WILMS' TUMOUR (NEPHROBLASTOMA)

Def: It is the malignant tumour of kidney that occurs in childhood (usually within first 3 years of life). It is usually unilateral, but may be bilateral.

Clinical features:

- May be asymptomatic.
- Abdominal mass.
- Rarely, haematuria.

Investigation:

- USG of whole abdomen.
- CT or MRI.
- Urine for RME (haematuria may be present).
- CBC, ESR (may be anaemia or even polycythaemia).
- USG or CT guided FNAC (if needed).

Treatment:

- In early stage (stage 1 and 2): Nephrectomy followed by chemotherapy (vincristine, dactinomycin, doxorubicin).
- In late stage (stage 3 and 4): Nephrectomy followed by chemotherapy (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide) and post-operative radiotherapy.

Prognosis: Overall, 5 year survival rate is 90%.

MASS IN LEFT OR RIGHT ILIAC FOSSA (TRANSPLANTED KIDNEY)

Instruction by the examiner:

- Examine the abdomen.
- Palpate the abdomen.

Presentation of a Case:

- There is a mass in right (or left) iliac fossa, 5×5 cm, non-tender, round in shape, surface is regular, with clear margin.
- There is a laparotomy scar (look for AV fistula in arm).

My diagnosis is **Transplanted kidney**.

Q: What is the **indication** of kidney transplantation?

A: End-stage renal disease (when GFR is <5 mL/min).

Q: What are the **causes** of CKD?

A: As follows:

- Diabetes mellitus (20 to 40%).
- Hypertension (5 to 20%).
- Tubulointerstitial diseases (20 to 30%).
- Glomerular diseases (10 to 20%) e.g., IgA nephropathy, mesangiocapillary glomerulonephritis (MCGN)
- Systemic inflammatory diseases (5 to 10%) e.g., SLE, vasculitis.
- Renal artery stenosis (5%).
- Congenital and inherited (5%) e.g., polycystic kidney disease, Alport's syndrome.
- Obstructive uropathy.
- Chronic pyelonephritis.
- Unknown (5 to 20%).

Q: From where kidney is **collected** for transplantation?

A: It is collected from:

- Matched cadaver donor.
- Relatives who are HLA-identical and ABO-matched.
- Brain dead person who are on ventilator.

Q: Where the transplanted kidney is **placed**?

A: In iliac fossa (either right or left). Donor renal vessels are anastomosed with recipient's external or internal iliac artery and vein. The donor ureter is placed into the recipient's urinary bladder.

Q:How do you **diagnose** acute rejection?

A: In the following way:

- Pain in the transplanted area.
- Reduction of urine output.
- Renal area is tender.
- Increased serum urea and creatinine.
- Urine shows plenty of RBC.
- USG shows reduced echogenicity.
- Isotope scan (^{99}TcM or DTPA) shows reduced uptake.
- Graft biopsy may be required.

Q:How to **manage** after rejection?

A: High dose steroid (short course) is given. Other therapies: anti-lymphocyte antibody or plasma exchange in resistant case.

Q:Is there any **bad effect** of repeated blood transfusion before kidney transplantation?

A: Repeated transfusion should be avoided as it carries risk of HLA sensitization. But pre-treatment with multiple transfusions from donor tends to increase graft survival (in contrast to bone marrow transplantation).

Q:What is **CKD** and what is **ESRD**?

A: As follows:

- Chronic kidney disease (CKD) is the irreversible deterioration of renal function that develops over a period of years. In CKD, GFR is >10 mL/min, medical treatment is still possible to maintain renal function.
- End-stage renal disease or failure (ESRD) is a stage when renal replacement therapy is compulsory by either dialysis or renal transplantation, without which death is likely. GFR is <5 mL/min and renal function cannot be maintained with medical treatment.

Q:What are the **contraindications** of renal transplantation?

A: As follows:

1. Absolute:
 - Active malignancy: A period of at least 2 years of complete remission is recommended for most tumours.
 - Active vasculitis or recent anti-GBM (anti-glomerular basement membrane) disease.
 - Severe heart disease or any severe co-morbid condition.
 - Severe occlusive aorto-iliac vascular disease.
2. Relative:
 - Age: While practice varies, transplants are not routinely done to children (<1 year) or older people (>75 years).
 - High risk of disease recurrence in the transplant kidney.
 - Disease of lower urinary tract: In patient with impaired bladder function or stricture urethra (an ileal conduit may be considered.)
 - Significant co-morbidity.

Q:What drugs are used to **prevent rejection** (or management after transplantation)?

A: combination of: prednisolone **plus** cyclosporine or tacrolimus **plus** azathioprine or mycophenolate mofetil or sirolimus or everolimus.

Q: What are the complications of immunosuppression?**A:** As follows:

- Infection (see below).
- Malignancy (see below).

Q: What are the complications after renal transplantation?**A:** As follows:**Early complication:****1. Acute rejection:**

- It occurs in 10 to 30% cases within 6 months.
- The patient presents with fever, loin pain, hypertension, swelling of the graft, rising creatinine.
- Urine shows protein, lymphocyte and renal tubular cells. Graft biopsy shows immune cell infiltrate and tubular damage.
- Treatment: High dose methylprednisolone (500 mg IV for 3 days). In resistant case, anti-thymocyte globulin (ATG), anti-lymphocyte globulin (ALG), OKT3, immunoglobulin, plasma exchange may be used.

2. Acute tubular necrosis: It is the commonest cause of cadaveric graft dysfunction (40 to 50%), associated with worse long term outcome and increases risk of graft rejection.**3. Technical failures:** Occlusion or stenosis of arterial anastomosis, occlusion of venous anastomosis and urinary leaks.**4. Infection:**

- Virus: Cytomegalovirus, polyoma virus.
- Parasite: Pneumocystis jirovecii.
- Fungus: Oral candidiasis.
- Bacterial: Common in first few months.

Late complication:**1. Post-transplantation lymphoproliferative disorder:** Epstein Barr virus associated malignancies (such as lymphoma) are common in patients who receive biological agents and in children.**2. Malignancy:** Skin tumour (e.g., basal and squamous cell carcinoma), renal, carcinoma of cervix and vaginal.**3. Cardiovascular:** Hypertension, atherosclerosis. Cardiovascular disease causes 50% death in transplanted patients.**4. Chronic rejection:**

- Usually occurs after 6 months.
- There is gradual rise of creatinine and proteinuria.
- Graft biopsy shows vascular change, fibrosis and tubular atrophy.
- It is not responsive to increased immunosuppression.

5. Complication of immunosuppressive drugs including steroid.**6. Post-transplantation osteoporosis** (may occur due to steroid).**7. Chronic allograft nephropathy:** common cause of late graft failure.**8. Recurrence of renal disease is common.** Such as:

- Primary focal segmental glomerulosclerosis.
- Mesangiocapillary glomerulonephritis.
- Diabetic nephropathy.
- IgA nephropathy.

Complication of renal transplantation (Remember the formula, 'TROPICAL'):

- **T**—Thrombosis of graft kidney artery and vein.
- **R**—Rejection of graft kidney.
- **O**—Obstruction of graft ureter with peri-nephric haematoma, seroma, urinoma or lymphocoele.
- **P**—Primary disease recurrence. Common recurrence is MCGN type-II (80 to 100%).
- **I**—Infection: Bacterial (any, tuberculosis), Viral (CMV, chicken pox, polyoma virus), fungal (*Cryptococcus neoformans*), Parasite (*Pneumocystis jirovecii*, isospora, cyclosporidium, microspora, giardia).
- **C**—Cyclosporine toxicity and other immunosuppressive drug toxicities.
- **A**—Acute tubular necrosis.
- **L**—Leakage of graft ureter (error or ischaemia).

Q: What are the **prognoses** after kidney transplantation?

A: As follows:

Survival in transplant from living donor:

- 1 year survival 85 to 90%.
- 3 year survival 70 to 75%.
- 5 year survival 60 to 65%.
- 10 year survival 50 to 55%.

Survival in transplant from cadaver donor:

- 96% patient survival and 93% graft survival at 1 year.
- 88% patient survival and 84% graft survival at 5 year.

N.B.: If the donor is genetically identical (e.g., an identical twin), immunosuppressive treatment may not be needed.

NEPHROTIC SYNDROME

Instructions by the examiner:

- Look at the face of this patient Or, perform general examination.

Presentation of a Case:

- The patient is grossly oedematous, face is puffy with baggy eyelids, pitting oedema is present.
- Mention if these are present: Leukonychia, signs of SLE or RA.

My diagnosis is **Nephrotic syndrome (NS)**.

Q: What else do you want to examine?

A: I want to examine the abdomen to see ascites, also chest to see any pleural effusion (which may be bilateral).

Q: What are your differential diagnoses?

A: As follows:

- Acute glomerulonephritis.
- Severe congestive cardiac failure.
- Cirrhosis of liver.
- Hypoproteinaemia due to any cause (such as malnutrition or malabsorption).



Nephrotic syndrome



Puffy face with baggy eyelids in nephrotic syndrome



Ascites and oedema in nephrotic syndrome

Q: What history would you like to take in any case of NS?

A: As follows:

- Diabetes mellitus (causing diabetic nephropathy).
- Drugs, such as captopril, NSAID, penicillamine.
- Malignancy (lymphoma, leukaemia).
- Skin rash, arthritis, arthralgia, alopecia (SLE).
- History of other diseases like malaria, leprosy, syphilis, hepatitis B virus, hepatitis C virus, amyloidosis, vasculitis.
- Family history of sickle cell disease, Alport's syndrome, nail patella syndrome.

Q: What **bedside test** do you like to do?

A: Urine examination (shows massive proteinuria).

Q: What **investigations** should be done in nephrotic syndrome?

A: As follows:

1. Urine R/E: Shows gross proteinuria. Red cells and red cell casts are absent (also urine sugar to exclude diabetic nephropathy).
2. 24 hours urinary protein (more than 3.5 g/24 hours is suggestive of nephrotic syndrome).
3. Serum total protein, serum albumin and A:G ratio (hypoalbuminaemia).
4. Serum lipid profile (high cholesterol and high triglycerides may be present).
5. Blood sugar, blood urea, serum creatinine, serum electrolytes should be done.
6. USG of the whole abdomen to look for renal pathology.
7. Other investigations: according to history and suspicion of cause
 - Blood sugar (to exclude diabetic nephropathy).
 - Chest X-ray (to exclude bronchial carcinoma, lymphoma; also to see bilateral pleural effusion, pericardial effusion).
 - ANA, anti-dsDNA (if suspicion of SLE).
 - p-ANCA and c-ANCA (if suspicion of vasculitis).
 - HBsAg and anti-HCV screening.
 - Complement C₃ and C₄.
 - Renal biopsy (to see the type of glomerulonephritis, whether minimal, membranous or membranoproliferative). This will guide for diagnosis, therapy and prognosis.

Q: What is **nephrotic syndrome**? What are the **causes**?

A: Nephrotic syndrome is characterized by generalized oedema, massive proteinuria and hypoalbuminaemia (with or without hyperlipidaemia). Causes are:

1. Primary renal disease: All glomerulonephritides (80%):
 - Minimal change glomerular disease (commonest in children).
 - Membranous GN (commonest in adult).
 - Mesangiocapillary and proliferative glomerulonephritis.
 - Focal and segmental glomerulosclerosis.
 - IgA nephropathy.
2. Secondary to other disease:
 - Diabetic nephropathy.
 - Collagen disease such as SLE, also rheumatoid arthritis (due to amyloidosis).
 - Amyloidosis.
 - Drugs: Penicillamine (common), captopril.
 - Neoplastic: Carcinoma (bronchial carcinoma), lymphoma.
 - Infection: Malaria (quartan malaria), bacterial endocarditis, HBV, HCV, HIV, secondary syphilis, leprosy.
 - Allergies: Bee stings, snake bite, anti-snake venom, pollens.

Q: What is the **commonest cause** of nephrotic syndrome in children and adult?

A: Commonest cause in children is minimal change glomerulonephritis and in adult is membranous glomerulonephritis.

Q: What are the lipid abnormalities in NS? What are the mechanisms?**A:** Lipid abnormalities are:

- Hypercholesterolaemia.
- High LDL, VLDL and IDL (HDL shows no change, or it may be low).

The mechanisms are:

- Increased synthesis of lipoproteins by the liver, secondary to hypoalbuminaemia.
- Reduced clearance of triglyceride rich lipoprotein (chylomicron and VLDL) in direct response to albuminuria.

As a result, there is high rate of atherosclerosis.

Q: What are the mechanisms of proteinuria?**A:** There is increased permeability of glomerular capillary due to:

- Reduction of fixed negatively charged protein molecules in glomerular capillary wall, which repels negatively charged protein molecules, allow proteins to pass through the pores.
- Damage to the glomerular basement membrane, leads to increase in size and number of pores, allowing passage of larger molecules.

Q: Why oedema in NS?**A:** Oedema is due to:

- Reduction of albumin causing low plasma oncotic pressure leading to oedema.
- Sodium retention in the extracellular compartment.
- Also, there is change in molecular barrier, which causes leakage of fluid.

Q: What is the blood pressure in NS?**A:** Usually BP is normal, even low. High BP may be secondary to underlying diseases like SLE with renal involvement, polyarteritis nodosa, diabetic nephropathy or terminal stage of nephrotic syndrome.**Q: How to treat nephrotic syndrome?****A:** As follows:**General measures:**

1. Fluid restriction: Depending on previous day's output and patient's oedema status (average 500 to 1000 mL/day).
2. Salt restriction (avoid extra salt).
3. Diuretics: Loop diuretics (frusemide, bumetanide). Potassium sparing diuretics (spironolactone) may be added.
4. Normal protein diet. High protein is not necessary, as it increases proteinuria and may be harmful.
5. Intravenous salt poor albumin may be given in diuretic resistant patients and in those with oliguria and uraemia in the absence of severe glomerular damage, e.g., in minimal change nephropathy. It helps in diuresis.
6. If infection: Antibiotic is given. Pneumococcal vaccine is recommended.
7. Venous thrombosis: To prevent, prolong bed rest should be avoided. Prophylactic heparin in immobile patient (enoxaparin may be given), followed by oral anticoagulant.
8. For hyperlipidaemia: Statin may be added.
9. ACE inhibitor or angiotensin II receptor antagonist is used in all types of GN (for their anti-proteinuric properties. These drugs reduce proteinuria by lowering glomerular capillary filtration pressure).

Specific measures:**1. In minimal change disease:**

- Prednisolone: 60 mg/m² body surface area (maximum 80 mg/day) for 4 to 6 weeks, followed by 40 mg/m² every alternate day for a further 4 to 6 weeks. More than 95% responds (in children). Alternately, prednisolone 1 mg/kg/day up to response (urine protein free) or 3 months followed by tapering the dose in next 3 months.
- If relapse after withdrawal of steroid, it should be given again with gradual withdrawal. Some patients may require low dose maintenance dose (5 to 10 mg/day) for 3 to 6 months.
- If frequent relapse or high dose steroid needed or incomplete response to steroid: Cyclophosphamide (1.5 to 2 mg/kg/day for 8 to 12 weeks) and prednisolone 7.5 to 15 mg/day should be given.
- An alternative to cyclophosphamide is ciclosporin 3 to 5 mg/kg per day, which is effective but must be continued long term to prevent relapse on stopping treatment.
- Rituximab may be used in frequent relapse.
- In corticosteroid-dependent children, the anthelmintic agent levamisole 2.5 mg/kg to a maximum of 150 mg on alternate days is also useful in maintenance of remission

2. For other treatment, see below (in glomerular disease).**Q: What is the prognosis in NS?****A: It depends on the type of NS.**

- Prognosis of minimal change disease in children is excellent. Remission and relapse may occur. CKD does not occur.
- In membranous nephropathy, 1/3rd may remit spontaneously, 1/3rd remains in nephrotic syndrome and 1/3rd shows progressive loss of renal function.
- In focal segmental glomerulosclerosis (FSGS) and mesangiocapillary GN: Prognosis is bad.
- IgA nephropathy: Course of the disease is indolent. ESRD occurs in 20 years.

Q: What are the complications of nephrotic syndrome?**A: As follows:**

1. Hypercoagulability leading to:
 - Venous thrombosis (especially renal vein thrombosis, also DVT).
 - Pulmonary embolism.
2. Infections: pneumococcal infection (may cause peritonitis and septicaemia), cellulitis, streptococcal, meningococcal infection etc.
3. Hyperlipidaemia leading to atherosclerosis.
4. Oliguric renal failure.
5. May cause bilateral pleural effusion, pericardial effusion.
6. Loss of thyroxin binding globulin that causes low FT₃ and FT₄.
7. Loss of transferrin and iron, resulting in iron deficiency anaemia.
8. Loss of vitamin D binding protein, leading to osteomalacia.

Q: If the patient develops **pain** in the loin, what is the likely diagnosis? How to **diagnose**?

A: Renal vein thrombosis. In nephrotic syndrome, if there is loin pain, haematuria and deterioration of renal function, it is highly suggestive of renal vein thrombosis.

It is more common in membranous nephropathy, mesangiocapillary glomerulonephritis and amyloidosis.

Investigation:

- Doppler ultrasound of renal vessels.
- CT or MRI.
- Sometimes renal angiogram may be done.

Treatment: Anticoagulant heparin for 5 to 7 days, then warfarin for 3 to 6 months.

Q: What are the **mechanisms of renal vein thrombosis** in nephrotic syndrome?

A: In nephrotic syndrome, there is hypercoagulable state due to:

- Loss of inhibitors of coagulation in urine such as antithrombin III, protein C and S.
- Loss of fibrinolytic factor (plasminogen).
- Increased synthesis of clotting factors: Factors V, VIII and fibrinogen.
- Other factors: Thrombocytosis and excessive diuresis causes dehydration, reduced renal blood flow and increased viscosity.

These predispose to increased venous thrombosis that occurs especially in renal vein.

BRIEF NOTES ON DIFFERENT GLOMERULONEPHRITIS CAUSING NEPHROTIC SYNDROME

MINIMAL CHANGE DISEASE (MCD OR MCN):

- Common cause of nephrotic syndrome in children, more in boys. But may occur in all ages.
- Proteinuria is highly selective, where albumin is lost in urine (but not high molecular weight proteins, immunoglobulins).
- On light microscopy, there is no abnormality. On electron microscopy, there is fusion of podocyte foot process.
- No immune deposit. Progression to renal failure is rare.
- Good response to steroid and cytotoxic drugs.

MEMBRANOUS GLOMERULOPATHY:

- Common cause of NS in adult, predominantly in male.
- Causes—Idiopathic. May be due to SLE, bronchial carcinoma, drugs (penicillamine), HBV, HCV.
- Renal vein thrombosis is a common complication.
- May progress to CKD.
- Renal biopsy shows thickening of glomerular basement membrane, increased matrix deposition and glomerulosclerosis. There is granular subepithelial IgG deposit.

Treatment:

- Cyclophosphamide (1.5 to 2.5 mg/kg per day for 6 to 12 months with prednisolone 1 mg/kg per day on alternate days for the first 2 months).
- Chlorambucil (0.2 mg/kg/day in months 2, 4 & 6, alternating with oral prednisolone 0.4 mg/kg/day in months 1, 3 & 5).
- Other drugs: Cyclosporin, tacrolimus, mycophenolate mofetil, rituximab may be used.

FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS):

- There is segmental scar in glomeruli, no acute inflammation, podocyte foot process fusion may be found. There is C3 and IgM deposition in the affected portions of glomerulus.
- Cause is unknown but may be related to HIV, heroin abuse, morbid obesity, reflux nephropathy, secondary to other GN.
- Mostly present as idiopathic NS. There is massive proteinuria, haematuria and hypertension.
- May progress to renal failure.

Treatment:

- Symptomatic and supportive.
- Steroid is effective in 40% cases. Prednisolone 0.5 to 2 mg/kg/day for 6 months.
- If no response: Mycophenolate mofetil 1 to 2 g/day or ciclosporine 5 to 6 mg/kg/day for 3 months, then dose is reduced and maintained up to 15 months.
- Tacrolimus 0.05 mg/kg/day may be given (occasionally effective).
- Cyclophosphamide, chlorambucil, azathioprine may be used.
- Renal transplantation can be done in renal failure, but may relapse after transplantation.

MESANGIOCAPILLARY GLOMERULONEPHRITIS (MCGN):

- Also known as membranoproliferative glomerulonephritis (MPGN), characterized by an increase in mesangial cells, thickening of glomerular capillary walls and subendothelial deposition of immune complex and complement.
- Causes: infection (hepatitis C), autoimmunity, subacute bacterial endocarditis, cryoglobulinaemia.
- Usual presentations are proteinuria and haematuria.
- 3 subtypes:
 1. **Type 1** (immunoglobulin type): Characterized by deposition of immunoglobulins within the glomeruli. It is associated with chronic infections, autoimmune diseases and monoclonal gammopathy.
 2. **Type 2** (Complement type): Characterized by deposition of complement in the glomeruli, associated with inherited or acquired abnormalities in the complement pathway. It is also called '**dense deposit disease**', in which there is deposition of electron-dense deposits within the GBM. This type is associated with partial lipodystrophy (loss of subcutaneous fat on face and upper trunk).
 3. **Type 3**: in which neither immunoglobulins nor complement are deposited in the glomeruli. This is associated with healing in HUS and TTP.

Treatment:

- In idiopathic MCGN (all age groups) with normal renal function and non-nephrotic range proteinuria: no specific therapy is required. Good blood pressure control, ideally with an ACE inhibitor, is of benefit.
- In **children** with the nephritic syndrome and/or impaired renal function: a trial of steroid is warranted (alternate day prednisolone 40 mg/m² for 6 to 12 months).
- In adult: Only symptomatic and supportive treatment. Aspirin or dipyridamole or both may be given.

READ THE FOLLOWING TOPICS IN RELATION TO NEPHROLOGY

Urinary incontinence: It means urine leaks involuntarily. It is of 4 types:

- Stress incontinence: Loss of urine with activity such as coughing, sneezing, lifting any object, exercise etc.
- Urge incontinence: Uncontrolled micturition preceded by strong urge to void urine. It is due to inflammatory condition or neurogenic bladder.
- Overflow incontinence: Usually in chronic urinary retention.
- Total incontinence: Patient loses urine at any time and at any position due to loss of sphincter efficacy.

Causes of red or dark urine:

- Haematuria (red).
- Haemoglobinuria (dark).
- Myoglobinuria (in rhabdomyolysis).
- Food dye (beet root).
- Drugs: Rifampicin (orange), L-dopa (dark on standing), clofazimine (red), phenolphthalein (pink), senna (orange).
- Acute intermittent porphyria (urine becomes dark, if kept for long time).
- Alkaptonuria (urine becomes black, if kept for long time).

Q: What is haematuria?

A: Passage of blood in urine is called haematuria. It may be macroscopic, microscopic, gross haematuria.

Q: What are the types of haematuria?

A: As follows:

- Initial haematuria: Presence of blood at the beginning of micturition, usually due to penile urethral cause.
- Terminal haematuria: Presence of blood at the end of micturition, usually due to bladder or prostatic urethral cause.
- Total haematuria: Presence of blood throughout micturition, usually due to bladder disease (transitional cell carcinoma), urinary tract disease or blood dyscrasia or excess anticoagulant.
- Intermittent haematuria: IgA nephropathy, Alport's syndrome, polycystic kidney disease, renal tumour.

Q: What are the causes of painless haematuria?**A:** As follows:

- Renal cell carcinoma.
- Polycystic kidney disease.
- Schistosomiasis.
- Renal TB.
- Tubulo-interstitial nephritis.
- Papilloma of urinary bladder.
- Carcinoma of urinary bladder.
- Benign hypertrophy of prostate.
- Bleeding disorder.
- Heparin, antiplatelet drug therapy.
- Infective endocarditis.
- Malignant hypertension.

Q: What are the causes of microscopic haematuria?**A:** As follows:

- Renal TB.
- Glomerulonephritis.
- Malignant hypertension.
- Infective endocarditis.
- Blood dyscrasia (haemophilia, Christmas disease).
- Benign prostatic hyperplasia.
- Polyarteritis nodosa.
- Wegener's granulomatosis.
- Good Pasture's syndrome.
- Alport's syndrome.

Q: What is haemoglobinuria?

A: Passage of haemoglobin in urine due to any cause is called haemoglobinuria. It occurs due to intravascular haemolysis due to any cause (such as falciparum malaria, cold agglutinin disease, paroxysmal nocturnal haemoglobinuria, microangiopathic haemolytic anaemia etc., March haemoglobinuria, prosthetic heart valve).

Q: How to differentiate between haematuria and haemoglobinuria?**A:** As follows:

Points	Haematuria	Haemoglobinuria
1. Urine	Red	Dark
2. Microscopy	RBC present	RBC absent

Q: What is myoglobinuria?

A: Passage of myoglobin in urine due to rhabdomyolysis or muscle destruction is called myoglobinuria. Urine is usually brown coloured. It is detected by ammonium sulphate test. Causes of rhabdomyolysis:

1. **Physiological:** heavy exercise, marathon runner,

2. Pathological:

- High fever.
- Trauma (crush injury).
- Heat stroke.
- Convulsion.
- Neuroleptic malignant syndrome.
- Infectious disease (influenza, Legionnaire's disease).
- Snake venom.
- Electrocution.
- Polymyositis.
- Septicaemia.
- Drug (ecstasy or amphetamine abuse).
- Alcohol.

Q: What are the causes of sterile pyuria?

A: As follows: (urine shows pus cells but is negative on culture):

- Renal tuberculosis.
- Non-gonococcal urethritis (chlamydia, ureaplasma).
- Schistosomiasis.
- Tubulointerstitial nephritis, analgesic nephropathy.
- Papillary necrosis.
- Polycystic kidney disease.
- Haemorrhagic cystitis (due to cyclophosphamide).
- Inadequately treated UTI.
- Prostatitis.
- Renal transplant rejection.

Q: What are the causes of nocturia?

A: As follows:

- Benign prostatic hyperplasia or prostatism.
- Oedematous state (such as CCF).
- Diabetes mellitus.
- Diabetes insipidus.
- Chronic kidney disease.
- Sickle cell disease.
- Diuretic taken in the evening or night.
- Excess night time fluid intake.
- Anxiety.
- Obstructive sleep apnoea.

Q: What is dysuria?

A: Dysuria refers to pain or discomfort during micturition. Most common cause is UTI.

Q: What is oliguria?

A: Passage of <300 mL urine per day is called oliguria.

Q: What is anuria?

A: Passage of <50 mL urine per day is called anuria.

Q: What is polyuria?

A: Passage of >3 litre urine per day is called polyuria. It should be differentiated from frequency, which means frequent passage of small amount of urine.

Q: What are the causes of proteinuria?

A: Normal daily urinary protein excretion is <150 mg. Causes of proteinuria are:

- A. Physiological:** Stress, fever, exercise, high protein intake, exposure to cold, orthostatic proteinuria.
- B. Pathological:**
 - **Renal:** any primary renal disease (nephrotic syndrome, acute glomerulonephritis, chronic Glomerulonephritis, IgA nephropathy, pyelonephritis, renal tubular acidosis, tubulo-interstitial nephropathy, renal tumour).
 - **Pre-renal:** High fever, CCF, cirrhosis of liver, systemic disease (such as DM, HTN, infective endocarditis, hepatitis B, HIV, quartan malaria, amyloidosis), toxemia of pregnancy, drugs (such as penicillamine, captopril, NSAID), burn, blood transfusion, post-operative, acute alcohol abuse.
 - **Post-renal:** Prostatitis, urethritis, cystitis, obstructive uropathy.

Q: What is orthostatic proteinuria?

A: When proteinuria occurs during prolonged standing but not on recumbent position. It is a benign condition, usually occurs below 30 years of age. In the absence of renal or other abnormality, no investigation is necessary.

Q: What is microalbuminuria?

A: It is defined as albuminuria 20 to 200 microgram/minute or 30 to 300 mg/day. It is detected in radio-immunoassay, not detected by conventional method. It is a predictor of early diabetic nephropathy (IDDM) in adults. Mortality is high due to ischaemic heart disease. It is more in HTN with DM. There is increased incidence of IHD with retinopathy.

Treatment: good control of DM, control of HTN (preferably with ACE inhibitor).

Q: What is selective and non-selective proteinuria?

A: As follows:

- Selective proteinuria: infiltration of low molecular weight protein like albumin through the glomerular membrane. It is found in minimal change disease.
- Non-selective proteinuria: passage of low (albumin) and high (e.g., immunoglobulin) molecular weight protein through glomerular membrane.

N.B.: Normal daily protein excretion is 150 mg in 24 hours.

NEUROLOGY

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NEUROLOGY

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'The man who confesses his ignorance shows it once, he who tries to conceal it shows many times'
—A Japanese Proverb

INTRODUCTION

Neurological cases are the most feared part in any examination. However, these cases are probably the most straightforward in terms of diagnosis and defining the site of lesion. To attain efficiency and skill, a good deal of practice is required that will suffice to score highly.

Candidates are expected to know: **'What is the lesion? What is the site of lesion? What is the cause of lesion'?**

The signs need to be elicited carefully for exact anatomical localization of any lesion. Examiners use to ask:

- Perform the neurological examination of lower limbs.
- Perform the neurological examination of upper limbs.
- Look at the leg. What is your finding? (may be wasting, fasciculation or pes cavus).
- Examine the hands (may be wasting or claw hands).
- Talk to the patient (may be dysarthria, dysphasia or hoarse voice).
- Look at the patient. What is your diagnosis? (may be Parkinsonian face or involuntary movement, e.g., tremor, chorea, athetosis, titubation).
- Examine the cranial nerves.
- Examine the facial nerve.
- Look at the face. What do you think the diagnosis? (Bell's palsy).

Occasionally, examiner may ask, **'Examine the legs or lower limbs'** (In such case, examine the legs thoroughly, also perform neurological examination).

One must remember that there may be **non-neurological** cases. Candidates often mistakenly perform the neurological examination only. Hence, never forget the non-neurological cases and examine properly, keeping these in mind.

In lower limb, non-neurological cases may be (look very carefully and diagnosis may be obvious):

- Swelling of knee joints (arthritis or effusion).
- Erythema nodosum.
- Pre-tibial myxoedema.
- Systemic sclerosis.
- Diabetic foot.
- Unilateral or bilateral leg swelling.
- Vasculitis.
- Purpura or ecchymoses.
- DVT.
- Cellulitis.
- Buerger's disease.
- Necrobiosis lipoidica diabetorum.
- Pseudohypertrophy of calf muscles.
- Bowing tibia (may be due to Rickets or Paget's disease or congenital anomaly).

Even if asked to perform neurological examination, quickly look carefully to exclude the above diseases. After good visual survey, if nothing is obvious, proceed for the neurological examination.

NEUROLOGICAL EXAMINATION OF LOWER LIMB

Most likely cases in the examination are:

- Spastic paraplegia or flaccid paraplegia.
- Peripheral neuropathy.
- Friedreich's ataxia.
- Motor neuron disease (MND).
- Old poliomyelitis.

Proceed as follows:

Introduce yourself, ensure that lower limbs are well exposed (with permission), patient lying in supine position.

N.B.: If urinary catheter, it indicates spinal cord compression or disease, due to multiple sclerosis, transverse myelitis.

Inspection:

- Wasting (mention whether of right, left or both, involving thigh or leg).
- Skin change (shiny, pigmented, rough, ulceration, hair loss, gangrene). See the tip of the toes and soles.
- One leg is smaller than the other (found in old poliomyelitis).
- Pes cavus (involving right or left or both feet).
- Fasciculation (if not visible, tap the muscle with your fingers).
- Swelling of calf muscles (pseudohypertrophy of calf muscles).
- Joint abnormality (deformity or swelling, signs of inflammation).

Palpation:

1. Bulk of the muscles (measure with tape from a particular point):
 - Unilateral wasting (in old poliomyelitis).
 - Generalized wasting (in MND, polyneuropathy, lower motor neuron lesion).
 - Isolated anterior wasting in thigh (in diabetic amyotrophy).
 - Wasting in the leg that stops suddenly at a certain level (in Charcot–Marie–Tooth disease).
2. Muscle tone: Tell the patient, 'Keep your limbs relaxed'. Now the examinee should do the following—
 - Lift the leg and allow it to fall.
 - Palpate the muscle and perform side to side movement of the limbs.
 - Lastly, passive movement of the limb (in irregular fashion—flexion and extension).
3. Test for clonus (ankle and patella).
4. Muscle power (against resistance): If any weakness, mention **grading of weakness**. To test, ask the patient to follow your instructions as follows:
 - Hip flexion: 'Raise your leg straight, do not let me push it down'. (Prime mover: iliopsoas—L₁ & L₂).
 - Hip extension: 'Push your leg down, do not let me pull it up'. (Prime mover: glutei muscles—L₄ & L₅).

- Hip adduction: 'Push your thighs inwards, do not let me move them apart'. (Prime movers: adductors of thigh, such as adductor longus, brevis and magnus—**L₂, L₃ & L₄**).
 - Hip abduction: 'Push your thigh outwards. Do not let me push them inward'. (Prime movers: gluteus medius and minimus, sartorius and tensor fasciae latae—**L₄, L₅ & S₁**).
 - Knee flexion: 'Bend your knees, do not let me straighten them'. (Prime mover: hamstrings such as biceps femoris, semimembranosus and semitendinosus—**L₅, S₁ & S₂**).
 - Knee extension: 'Straighten your knees, do not let me stop doing'. (Prime mover: quadriceps femoris—**L₃ & L₄**).
 - Plantar flexion of ankle: 'Push your foot downwards against my hand'. (Prime movers: gastrocnemius, plantaris and soleus—**S₁ & S₂**).
 - Dorsiflexion of ankle: 'Push your foot upwards against my hand'. (Prime movers: tibialis anterior, extensor digitorum longus and extensor hallucis longus—**L₄ & L₅**).
 - Inversion of foot: 'Push your foot inward against my hand'. (Prime movers: tibialis anterior and posterior—**L₅ & S₁**).
 - Eversion of foot: 'Push your foot outward against my hand'. (Prime movers: peroneus longus and brevis—**L₅ & S₁**).
 - Extension of great toe: 'Push your great toe upwards and do not let me push it down'. (Prime mover: extensor hallucis longus—**L₅**).
5. Reflexes:
- Knee (**L₃** and **L₄**).
 - Ankle (**S₁** and **S₂**).
 - Plantar (**L₅, S₁** and **S₂**): Tell the patient, 'I am going to tickle the bottom of your foot, with an orange stick at the outer portion of the sole'. Mention your finding, 'Plantar is extensor or flexor or equivocal or cannot be elicited'.
- N.B.: Remember the following points:*
- If reflexes are absent, **never forget to do reinforcement**. Ask the patient to pull his or her clasped hands outwards (Jendrassik's manoeuvre), or clench the teeth and then see the reflex again.
 - Examine for **Oppenheim** sign (by pressing heavily the shin along the inner border of tibia going down) and **Gordon** sign (by squeezing the Achilles tendon). There will be extensor plantar response, if the signs are positive (indicates extensive pyramidal lesion).
6. Superficial reflexes:
- Abdominal reflex (**T₆** to **T₁₁**): Elicited by lightly stroking the abdominal wall diagonally towards umbilicus in each of the four quadrants of abdomen. If positive, reflex contraction of abdominal wall occurs. It is absent in upper motor neuron lesion (early loss is found in multiple sclerosis).
 - Cremasteric reflex (**L₁ & L₂**): Stroke the inner part of thigh in downward direction. Normally, contraction of cremasteric muscles pulls up the scrotum and testis on the side stroked.
7. Co-ordination (Explain and show it to the patient.):
- Heel–shin test: 'Please raise your leg, put your heel upon the knee of other leg and run it along the shin'. (Repeat the same for other leg).
 - Foot taping test: Keep your hand at a little distance from ball of patient's foot and ask the patient to tap it rapidly on your hand (dysdiadochokinesis).

8. Sensory test: Explain to the patient with light touch by cotton-wool in normal area such as forehead. Ask the patient 'Can you feel it'? Now touch the leg or foot. Ask the patient, 'Can you feel it'? If no, continue to touch above, until the patient can feel to find out the level of sensory loss.

- Light touch (cotton-wool).
- Pin prick.

Perform the test according to the nerve distribution:

- Outer thigh L2 (upper thigh).
 - Inner thigh L3 (also around knee).
 - Outer leg L5 (up to medial foot).
 - Inner leg L4.
 - Medial foot L5.
 - Lateral foot S1.
- Vibration sense (with 128 Hz tuning fork): Always explain the patient first by plucking a tuning fork and placing it over sternum. Then repeat it without vibration. Now, test is done placing the vibrating fork on bony prominence such as side of great toe, medial malleolus. If impaired, it may also be tested in knee and anterior superior iliac spine.
- Position sense (in great toe, always explain this to the patient.)
9. Test for proximal myopathy: ask the patient to stand up from sitting without support. Unable to do in proximal myopathy.
10. Test for Rombergism: Ask the patient to stand with feet together and close the eyes. In positive case, the patient tends to sway or fall. Be careful to protect the patient from falling. If positive, indicates sensory ataxia, dorsal column lesion (e.g., subacute combined degeneration, tabes dorsalis). In cerebellar lesion, positive in both closed and open eyes.
11. Gait:
- Ask the patient to walk, look any abnormality such as hemiplegic gait, foot drop, scissor gait.
 - Look for festinant gait. Also ask to turn quickly (in Parkinsonism, unable to turn quickly).
 - Ask the patient to walk heel-to-toe (to exclude midline cerebellar lesion, in which ataxia may be present).
 - Ask the patient to walk on toes (S_1 lesion will make it impossible).
 - Ask the patient to walk on heel (L_4 and L_5 lesion will make it impossible).
12. Finally, look at the spine to see any deformity, scar, gibbus and local tenderness.



Heel to toe walking



Walking on toes



Walking on heel

READ THE FOLLOWING TOPICS CAREFULLY

Grading of muscular weakness, Medical Research Council (MRC) criteria:

- **Grade 0:** Complete paralysis.
- **Grade 1:** A flicker of contraction only.
- **Grade 2:** Power detectable, when gravity is excluded by postural adjustment.
- **Grade 3:** Limb can be held against gravity, but not against examiner's resistance.
- **Grade 4:** There is some degree of weakness.
- **Grade 5:** Normal power.

Q: What are the sites of UMN lesion?

A: In the:

- Cerebral cortex.
- Internal capsule.
- Brainstem.
- Descending tracts up to anterior horn cells of spinal cord.

Q: What are the sites of LMN lesion?

A: In the motor pathway from anterior horn cells (or cranial nerve nucleus) via peripheral nerve to motor end plate.

Signs of upper motor neuron (UMN) lesion:

- Weakness or paralysis.
- Increased tone (hypertonia, spastic, may be clasp knife).
- Exaggerated tendon reflex, may be clonus and absent abdominal reflex.
- Plantar response: Extensor.
- No wasting (occasionally due to disuse).
- Normal electrical excitability of muscles.
- Upper limb drift: Present (see below).

Signs of lower motor neuron (LMN) lesion:

- Weakness or paralysis (flaccid).
- Hypotonia.
- Loss of all reflexes.
- Wasting of involved muscles.
- Fasciculation of affected muscles.
- Plantar: Normal or absent.

Signs of extrapyramidal lesion:

- Rigidity (leadpipe or cogwheel).
- Hypokinesia or bradykinesia (poverty of movement) or akinesia (no movement).
- Involuntary movements (tremor, chorea, athetosis, dystonia, hemiballismus).

Causes of hypertonia:

- UMN lesion (spastic, may be clasp knife).
- Extrapyramidal lesion (leadpipe or cogwheel).
- Conversion disorder (rigidity continues to increase with more and more passive movement).
- Others: Catatonic state, tetanus and strychnine poisoning.

Causes of hypotonia:

- LMN lesion (due to any cause).
- Cerebellar lesion (knee jerk may be pendular).
- Dorsal column lesion.
- Polyneuropathy.
- Hypokalaemia or hyperkalaemia.
- Drug: Any muscle relaxant.

Q: What is upper limb drift?

A: Normally, outstretched hands in front are held symmetrically even when the eyes are closed. In UMN lesion, when the upper limbs are outstretched with the palm uppermost, affected limb drifts downwards and medially, forearm tends to pronate and hands flex slightly at fingers.

Q: How reinforcement helps or acts?

A: Reinforcement acts by increasing the excitability of anterior horn cells and by increasing the sensitivity of muscle spindle primary sensory endings to stretch by increased gamma fusimotor drive.

Q: What are the causes of loss of tendon reflex?

A: As follows:

- LMN lesion.
- Peripheral neuropathy.
- Dorsal column lesion.
- Hypokalaemia or hyperkalaemia.

Isolated **loss of jerk** indicates radiculopathy of the affected segment (such as disc prolapse):

- Loss of biceps (C_{5,6} lesion).
- Loss of triceps (C_{6,7} lesion).
- Loss of ankle jerk (S₁ lesion).

Q: What are the causes of extensor plantar response?

A: As follows:

- First year of life (due to lack of myelination of pyramidal tract. Myelination occurs in 6 to 12 months).
- Sleep.
- UMN lesion.
- Deep coma (due to any cause).
- Postepileptic period (after grand mal seizure).

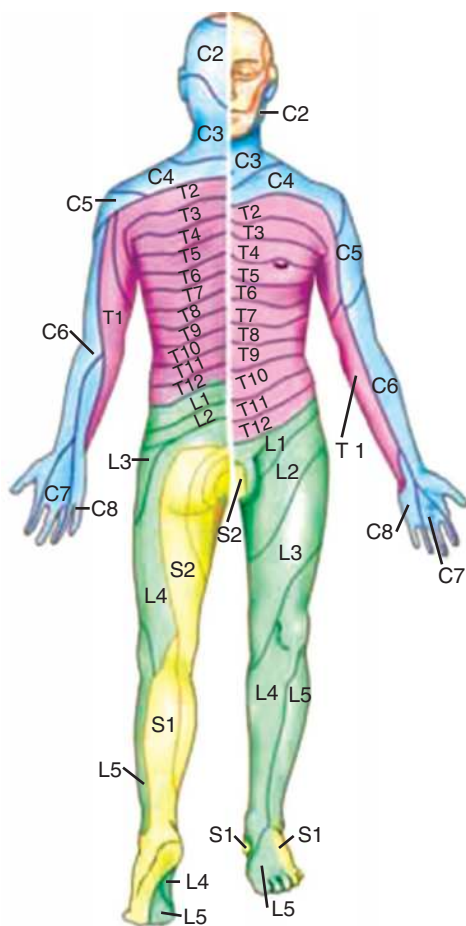
Q: What is Babinski sign?

A: It is the extensor plantar response characterized by extension of great toe with fanning of other toes (UMN lesion).

Q: What are the causes of **absent ankle jerk, but extensor plantar response**?

A: As follows:

- Subacute combined degeneration of spinal cord.
- Friedreich's ataxia.
- Multiple sclerosis.
- Taboparesis.
- Peripheral neuropathy with cervical myelopathy.
- Peripheral neuropathy in a stroke patient.
- Lesion in conus medullaris (cauda equina).
- Motor neuron disease (if UMNL and LMNL occurs in the same limb).



Dermatomes of human body (anterior and posterior)

SPASTIC PARAPLEGIA (SPINAL CORD COMPRESSION)

Instruction by the examiner:

- Examine the lower limbs or perform the neurological examination of the lower limbs.

Proceed to examine the lower limbs as described before. If there is any sensory loss, find out the level. Always look at the back to find any scar, bony deformity and gibbus or local tenderness in spine. Later, examine the upper limbs also.

Presentation of a Case:

- There is some wasting of right or left, or both thigh or leg (mention, if any).
- Both flexor and extensor muscles are weak (mention grade).
- There is hypertonia in both lower limbs (may be clasp knife, mention if any).
- Knee and ankle jerks are exaggerated with extensor plantar response on both sides.
- There is ankle clonus in right or left or both (mention, if any).
- Co-ordination is impaired in right or left or both (mention, if any).
- Loss of sensation in both lower limbs (mention, up to where).
- Vibration and position senses are normal.
- Scissor gait is present but Rombergism is absent.
- Examination of the back shows no spinal deformity or tenderness or any surgical scar over the spine.

My diagnosis is **Spastic paraplegia**, more likely due to spinal cord compression.

N.B.: There is no muscle wasting in UMN lesion. If wasting is present in spastic paraplegia, it is more likely due to disuse or prolonged immobilization.

Q: What are the **causes** of spastic paraplegia?

A: As follows (remember the age and also sensory loss):

- Spinal cord compression due to any cause (see below).
- Demyelinating disease (such as multiple sclerosis).
- Motor neuron disease (in middle aged or elderly).
- Friedreich's ataxia (in early age).
- Hereditary spastic paraplegia.
- Subacute combined degeneration of spinal cord.

Q: What are the **cardinal signs** of spinal cord compression?

A: As follows:

- UMN signs.
- Segmental sensory loss (sensory loss up to a particular segmental level).

Q: What are the **other features** of spinal cord compression?

A: As follows:

- Sphincter disturbance: Common (urinary retention and loss of bladder control).
- Root pain: Frequent at the site of compression.
- Pain radiates in a band around the chest (in thoracic cord compression).

Q: Can it be motor neuron disease?**A:** Unlikely, because in MND there will be:

- No sensory loss (very important sign).
- Fasciculation.
- Age (usually above 40 years).

Q: Can it be Friedreich's ataxia?**A:** Unlikely, in Friedreich ataxia:

- Early age.
- Pes cavus and kyphoscoliosis.
- Loss of knee and ankle jerk, plantar is extensor.
- Signs of cerebellar lesion.
- Signs of posterior column lesion (loss of vibration and position sense).

Q: What are the other findings in Friedreich ataxia?**A:** Optic atrophy, high arched palate, deafness and cardiomyopathy.**Q: Can it be subacute combined degeneration?****A:** Unlikely, as in SCD there will be:

- Peripheral neuropathy.
- Posterior column lesion (loss of vibration and position sense).
- Knee and ankle jerk absent (knee jerk may be brisk, plantar may be extensor).
- Romberg sign is positive.
- Others: Anaemia and smooth shiny tongue with atrophy of papilla.

N.B.: Remember to diagnose the cause of spastic paraplegia:

- *If spastic paraplegia with sensory loss with a definite upper limit: It is due to spinal cord compression.*
- *If plantar response is extensor, sensory loss is glove and stocking pattern with loss of vibration and position sense: It is due to SCD.*
- *If cerebellar signs are present: It is due to multiple sclerosis or Friedreich's ataxia.*
- *In young patient with pes cavus, dorsal column lesion and cerebellar signs: It is due to Friedreich's ataxia.*
- *If spastic paraplegia, but no sensory loss: It is due to MND (amyotrophic lateral sclerosis, also LMN lesion in upper limb).*

Q: What are the causes of paraplegia of sudden onset?**A:** As follows:

- Trauma (to vertebral column).
- Collapse of vertebra due to any cause.
- Multiple sclerosis.
- Anterior spinal artery occlusion.
- Dissecting aneurysm.
- Haematomyelia.
- Acute transverse Myelitis (may be due to post-infectious or post-vaccinal).

Q: What are the **causes** of spastic paraplegia?

A: As follows (**7 T's**):

- Trauma.
- Tuberculosis (Pott's disease).
- Tumour (meningioma, neurofibroma, lymphoma, leukaemia, myeloma, glioma, secondary deposit).
- Transverse myelitis.
- Tabes dorsalis.
- Twelve (B₁₂ deficiency).
- Thrombosis of anterior spinal artery.



Gibbus in tuberculous spondylitis



Cerebral palsy—spastic diplegia

Q: What is **mass reflex**?

A: After stimulation of skin of lower limbs or lower abdominal wall, there is reflex flexion of lower trunk muscles and lower limbs, evacuation of bladder, bowel and semen with sweating, called mass reflex. It indicates severe spinal cord lesion.

Q: What are the **causes** of spinal cord compression?

A: As follows:

1. Extradural (lesion in vertebral column):
 - Trauma.
 - Tuberculosis of spine (Pott's disease).
 - Secondary deposit (elderly).
 - Multiple myeloma (elderly).
 - Abscess (para-vertebral).
 - Lymphoma.

2. Intradural (extramedullary and intramedullary):**a) Extramedullary causes (within dura):**

- Meningioma.
- Neurofibroma.
- Secondary deposit (elderly).
- Lymphoma.
- Leukaemia.

b) Intramedullary causes:

- Glioma.
- Ependymoma.
- Syringomyelia.
- Haematomyelia.

Q: How to **find out** the sensory level in spinal cord compression?

A: In the following ways:

Vertebral Level	Spinal Cord Segment
1. Cervical vertebrae	Add 1
2. Upper-thoracic vertebrae (T ₁ to T ₆)	Add 2
3. Mid-thoracic vertebrae (T ₇ to T ₉)	Add 3
4. Xth thoracic vertebra	Lumbar 1 and 2
5. XIth thoracic vertebra	Lumbar 3 and 4
6. XIIth thoracic vertebra	Lumbar 5
7. First lumbar vertebra	Sacral and coccygeal cord segments

Q: What are the cerebral **causes** of spastic paraplegia?

A: As follows:

- Parasagittal meningioma (usually involving falx meningioma).
- Thrombosis of superior longitudinal sinus.
- Thrombosis of unimpaird anterior cerebral artery.
- Multiple cerebral infarctions.
- Hydrocephalus.
- Trauma.
- In children, cerebral palsy (cerebral diplegia, usual lesion is bilateral parasagittal cortical lesion).

Q: What are the **features** of paraplegia due to cerebral lesion?

A: As follows:

- Bladder disturbance (urinary retention).
- Cortical type of sensory loss.
- Other features: Headache, vomiting, convulsion, Jacksonian fit.

N.B.: Lower limbs and micturition centre are represented in the paracentral lobule. Hence, lesion in this area produces paraplegia associated with bladder dysfunction.

Q: What are the **non-compressive causes** of spastic paraparesis or paraplegia?

A: As follows:

- MND (e.g., amyotrophic lateral sclerosis).
- Subacute combined degeneration.
- Acute transverse myelitis.
- Multiple sclerosis.
- Friedreich's ataxia.
- Syringomyelia.
- Vascular disease of the cord.
- Hereditary spastic paraplegia.
- Tropical spastic paraplegia.
- Post-vaccination.
- Infective: Syphilitic amyotrophy, HIV, Herpes zoster, Herpes simplex.
- Non-metastatic manifestation of malignancy.
- Others: Radiation myelopathy, functional, lathyrism.

According to the type of lesion:

- Demyelinating: Multiple sclerosis, acute demyelinating encephalomyelitis (ADEM).
- Inflammatory: Sarcoidosis, post-viral, post-vaccinal.
- Infective: HIV, Herpes zoster, Herpes simplex, syphilis.
- Degenerative: MND, familial spastic paraplegia, SCD, Friedreich's ataxia.
- Vascular: Anterior spinal artery infarction, intramedullary haemorrhage, spinal arteriovenous malformation (AVM).
- Toxic: Lathyrism, radiation.

Q: What are the **differences** between compressive and non-compressive paraplegia?

A: As follows:

Topic	Compressive	Non-Compressive
1. Onset	Gradual	May be acute
2. Symmetry	Asymmetrical	Usually symmetrical
3. Root pain	Present	Absent
4. Bony deformity	Present	Absent
5. Bony tenderness	Present	Absent
6. Hyperaesthesia or girdle-like sensation	Present	Absent
7. Upper level of sensory loss	Present	Absent
8. Flexor spasm	Common	Uncommon
9. Bladder and bowel involvement	Usually early feature	Late feature, may be early in acute transverse myelitis.

Q: What investigations are done in spastic paraplegia? How to treat?**A:** As follows:

- X-ray of dorsolumbar spine (anteroposterior and lateral view).
- CT scan or preferably MRI of spine.
- Lumbar puncture and CSF study in some case.
- Other tests according to suspicion of cause (e.g., tuberculosis and multiple myeloma).

Treatment:**1. General measures:**

- Physiotherapy.
- Nutritional support.
- Care of bowel and bladder (if needed, catheterization).
- Change of position to prevent bedsores. Special bed may be used.
- For spasm: Baclofen, tizanidine, gabapentin, botulinum toxin etc. Intrathecal baclofen or phenol may be tried.

2. Specific measures:

- Neurosurgical intervention: In some cases.
- Orthopaedic measures.
- Treatment of primary cause.

Q: What is paraplegia in flexion and paraplegia in extension?**A:** As follows:

- **Paraplegia in flexion:** flexor muscles are spastic causing flexion of the lower limbs (hip and knee flexed, feet are dorsiflexed). It is due to complete transection of spinal cord. Both pyramidal and extrapyramidal tracts are affected.
- **Paraplegia in extension:** extensor muscles are spastic causing extension of the lower limbs (hip and knee extended, feet plantar flexed). It is due to involvement of pyramidal tracts from partial transection of spinal cord, but the extrapyramidal tracts (especially vestibulospinal tracts) are intact. May change to paraplegia in flexion if the damage to the spinal cord is more extensive and vestibulospinal tracts are destroyed.

Paraplegia in extension and paraplegia in flexion follows severe injury to the spinal cord.

Q: What are the differences between paraplegia in extension and flexion?**A:** As follows:

Points	Paraplegia in Extension	Paraplegia in Flexion
1. Cause	Pyramidal lesion	Pyramidal and extrapyramidal
2. Hypertonia	More in extensor group of muscles	More in flexor group of muscles
3. Position of lower limbs	Extended	Flexed
4. Deep reflexes	Exaggerated	Less exaggerated
5. Clonus	Present	Absent
6. Mass reflex	Absent	May be present
7. Bladder	Precipitancy	Automatic bladder

Q: What is the **difference** between rigidity and spasticity?

A: As follows:

1. Spasticity means increased resistance during the initial part of passive movement, followed by lessening of the resistance. It may be clasp-knife type, in which there is more resistance at the onset of movement followed by sudden loss of resistance. It is due to pyramidal lesions. It is associated with other signs of UMN lesion. It involves only the antigravity muscles (extensors of the upper limbs and flexors of the lower limbs).
2. Rigidity means sustained uniform resistance during passive movement. It is due to extrapyramidal lesion and involves all groups of muscles. It may be:
 - Lead pipe in which resistance is uniform throughout the passive movement (better seen in elbow and knee).
 - Cog wheel in which continuous resistance is interrupted by tremor (better seen in the wrist and ankle joints).

Q: What are the findings of spinal cord compression at different **levels** of spinal cord?

A: As follows:

- **Lesion above C₅:** UMN lesion in both upper and lower limbs with loss of sensation in all four limbs.
- **Lesion at C₅:** LMN lesion in proximal muscles of upper limbs (rhomboid, deltoid, biceps, brachioradialis) with segmental loss of sensation and UMN lesion in rest of the upper limbs and in lower limbs. Biceps reflex is lost and triceps jerk is exaggerated.
- **Lesion at C₈:** LMN lesion and wasting of the intrinsic muscles of the hand and UMN lesion in lower limbs. There is segmental loss of sensation.
- **Lesion in thoracic cord:** Spastic paraplegia with segmental sensory loss. Loss of upper abdominal reflexes at T₇ and T₈. Loss of lower abdominal reflexes and upward displacement of umbilicus at T₁₀ and T₁₁.
- **Lesion at L₁:** UMN lesion in lower limbs and cremasteric reflex is lost (normal abdominal reflex).
- **Lesion at L₄:** LMN lesion and wasting of quadriceps, loss of knee jerk but hyperreflexia of ankle jerk and extensor plantar response.
- **Lesion in L₅ and S₁:** LMN lesion causing weakness of knee flexion and hip extension (S₁) and abduction (L₅) plus calf and foot muscles. Knee jerk is present, but no ankle jerk or plantar response. Anal reflex is present.
- **Lesion in S₃ and S₄:** No anal reflex, saddle sensory loss, normal lower limbs.

MULTIPLE SCLEROSIS (PRESENTING AS SPASTIC PARAPLEGIA)

Instruction by the examiner:

- Perform neurological examination of lower limbs.

Presentation of a Case: Presents as described in spastic paraplegia plus there may be slight sensory abnormality, but no definite upper limit (may be loss of vibration and position sense, mention if any).

My diagnosis is **Spastic paraplegia which may be due to:**

- Spinal cord compression due to any cause (see below).
- Demyelinating disease (such as multiple sclerosis).
- Motor neuron disease (in middle aged or elderly).
- Subacute combined degeneration.

Q: Why not spinal cord compression?

A: No definite upper limit of sensory loss.

Q: If it is multiple sclerosis, what **relevants** do you want to see?

A: As follows:

- Eye: Nystagmus and optic neuritis or optic atrophy.
- Signs of cerebellar lesions (see in 'Cerebellar Lesion' in this chapter).
- Abdominal reflex (early loss).
- Urinary incontinence, impotence and constipation (**triad of Steinberg**).

Q: What are the **causes** of bilateral upper motor neuron lesion involving the lower limbs?

A: As follows:

- Spinal cord compression.
- Multiple sclerosis.
- MND (amyotrophic lateral sclerosis).
- Hereditary spastic paraplegia.
- Transverse myelitis.
- Subacute combined degeneration.
- Friedrich's ataxia.
- Bilateral cerebral infarction.
- Cervical myelopathy.

Q: What are the **common modes of onset** of MS?

A: As follows:

1. Optic neuritis (25%).
2. Transverse myelitis (like spinal cord compression).
3. Cerebellar ataxia.
4. Various brainstem syndromes: Vertigo, facial pain or numbness, dysarthria, diplopia.

Q: What are the presentations of MS?

A: Twice more common in females. Age of onset is 20 to 45 years. It is rare before puberty and after 60 years. The patient usually presents with:

- Weakness of one or more limbs.
- Optic neuritis (patient complains of blurring of vision).
- Features of spastic paraplegia (confused with spinal cord compression).
- Features of cerebellar signs (ataxia and tremor etc.).
- Features of brainstem dysfunction (vertigo, diplopia, nystagmus, facial numbness or weakness, dysarthria, dysphagia and pyramidal signs in limbs).
- Bladder dysfunction (incontinence, dribbling, hesitancy).
- Sensory disturbance: Tingling of the limbs and light banding sensation around the trunk or limbs (due to posterior column involvement). There may be loss of vibration sense and proprioception in feet. Hand may also be involved.
- Euphoria despite disability.
- Others (rarely): Epilepsy, trigeminal neuralgia, facial palsy (may be recurrent), VIth nerve palsy, tonic spasm or brief spasm of limbs, dementia, neuropsychiatric dysfunction, depression, progressive non-compressive paraparesis, partial Brown–Séquard syndrome, internuclear ophthalmoplegia with ataxia.

Signs and symptoms of MS (remember the mnemonic: WATSON)

- **W:** Weakness (in one or more limbs, or generalized, after hot bath).
- **A:** Ataxia (cerebellar).
- **T:** Tremor (cerebellar).
- **S:** Speech (scanning).
- **O:** Optic neuritis.
- **N:** Nystagmus.

Q: What investigations should be done in MS?

A: As follows:

1. MRI of brain and spinal cord: Investigation of choice (CT scan is not sensitive).
2. Lumbar puncture and CSF study. There is slight increase in lymphocyte, increase in total protein in 40% cases and oligoclonal band in 70 to 90% cases, mainly IgG on electrophoresis.
3. Evoked potential: Mainly VEP (visual evoked potential) is usually delayed, if optic nerve involvement.
4. To exclude other disease:
 - Chest X-ray (to exclude bronchial carcinoma).
 - X-ray of spine (to exclude cord compression).
 - Serum B₁₂ (to exclude subacute combined degeneration of spinal cord).
 - ANA (to exclude SLE).
 - Antiphospholipid antibody.

Q: What is the **role of MRI**? What are the **findings** in MRI?

A: MRI is the single most investigation to confirm multiple sclerosis, positive in 80% cases. It shows multiple plaques, hyperintense in T2W and FLAIR mainly in the periventricular region, corpus callosum, cerebellar peduncles, juxtacortical posterior fossa, brainstem and subpial region of spinal cord. Although, these are typical, but not pathognomonic and may be found in small infarcts, disseminated metastases, Moyamoya disease and inflammatory diseases.

READ THE FOLLOWING TOPICS IN RELATION TO MULTIPLE SCLEROSIS

Q: What is **MS**? What is the **natural history** of the disease?

A: It is a demyelinating disorder of central nervous system characterized by focal neurological lesions disseminated in both time and space, with recurrence and remission over a period of many years and usually progressive. There are multiple plaques of demyelination within the brain and spinal cord, gliosis, varying degrees of inflammation and neuronal loss. Usually there is relative preservation of axons.

Natural history is extremely variable—may be acute, subacute, insidious, relapsing and remitting, chronic progressive, spontaneous recovery, rapidly progressive and secondarily progressive.

It is also called disseminated sclerosis, as the plaques are **disseminated both in time and space**. Presence of two neurological lesions in anatomically unrelated sites or at different times indicates MS.

Q: What are the **clinical courses (or types)** of MS?

A: As follows:

- **Relapsing and remitting MS** (85 to 90%): The patient suffers from episodes of acute attack with recovery and remains stable between relapses.
- **Primary progressive MS** (10 to 15%): Gradual neurological deterioration from the onset, after 40 years (late onset).
- **Secondary progressive MS:** Some cases of relapsing and remitting course show gradual neurological deterioration, may be superimposed acute relapses.
- **Relapsing progressive MS** (<5%).

Q: What are **sites of involvement** in MS?

A: As follows:

- Optic nerve.
- Brainstem.
- Cerebellum.
- Periventricular region.
- Spinal cord (posterior column and corticospinal tract).

Q: What are the **features** of end stage MS?

A: In end stage disease, the patient is severely disabled with spastic paraplegia, tetraplegia, ataxia, optic atrophy with blindness, pseudobulbar palsy, urinary incontinence, brainstem dysfunction and dementia.

Q: What are the other demyelinating disorders?**A:** As follows:

- Devic's disease (acute necrotizing myelitis with optic neuritis).
- Tuberous sclerosis (patchy demyelination).
- Leukodystrophies.
- Schilder's disease (diffuse cerebral sclerosis). There may be cortical blindness if occipital cortex is involved. Other features are cerebral deafness, quadriplegia, hemiplegia, dementia, pseudobulbar palsy.
- Acute disseminated encephalomyelitis (ADEM).

Q: What are the prognostic factors in MS?**A:** As follows:**1. Good prognostic factors:**

- Early age of onset.
- Relapsing and remitting form of disease.
- Visual or sensory symptoms alone at presentation.
- Minimum neurological impairment 5 years after onset.
- More benign course in women than in men.
- Little residual disability 5 years after onset.

2. Poor prognostic factors:

- Old age >40 years.
- Frequent relapse in the first 2 years.
- Short interval between first two relapses.
- Pyramidal, brainstem and cerebellar symptoms.
- Primary progressive disease.
- Poor recovery from relapse.
- MRI shows many lesions.

Q: What is Uhthoff phenomenon?

A: Exaggeration of symptoms after hot bath is called Uhthoff phenomenon. The patient feels extreme weakness after hot bath. It is due to heat induced conduction block of partially demyelinated fibres.

Q: What is Lhermitte sign?

A: When the neck is flexed, there is tingling or electric shock like sensation or funny sensation that passes down in the upper limb, trunk and perhaps lower limbs, called Lhermitte sign (also called barber's chair sign). It indicates that the disease is near the dorsal column nuclei of higher cervical cord (indicates cervical cord compression). Causes are:

- MS (common cause, especially in acute exacerbation).
- Cervical spondylosis.
- Cervical cord compression (by tumour).
- Subacute combined degeneration.
- Radiation myelopathy.
- Cervical spondylotic myelopathy.

*N.B.: A similar sensation by neck extension may occur called **reverse Lhermitte sign**. It strongly suggests cervical spondylosis.*

Q: What happens during **pregnancy** in MS?

A: Mild protective effect during pregnancy. Exaggeration may occur in puerperium.

Q: What are the **causes** of MS?

A: Unknown, the following factors may be associated:

- Environmental factors: More in temperate zone, rare in tropical country. Also more among rural than urban dwellers.
- More frequent in the higher socioeconomic group.
- Genetic: Ten times more in first degree relative.
- Immunological: There is an increase in activated T-lymphocyte in CSF, increase in immunoglobulin in CNS and increase in antibody to some virus (measles).
- Diet: More in those who eat animal fat.
- Lack of vitamin D and lack of exposure to sunlight may be a risk factor.
- HLA association—DR2, DR3, B7, A3.

Q: How to **treat** MS?

A: As follows:

1. During acute attack:

- Intravenous methylprednisolone: 1 g for 3 days or oral 500 mg for 5 days. It shortens the duration of relapse but does not affect the long term outcome. It is followed by oral prednisolone 40 mg daily for 10 days, then 20 mg for 2 days and then 10 mg for 2 days.
- Or, high dose prednisolone: 40 to 60 mg daily for 10 days, then tapered over for 2 days (it has no role for long term use for prevention).
- Plasmapheresis is sometimes helpful in patient with severe relapse and unresponsive to corticosteroid.

2. To prevent relapse (disease modifying drugs may be given):

- Immunosuppressive drug: Azathioprine may be helpful (cyclophosphamide, sometimes helpful in aggressive disease, is not recommended for widespread use). Mitoxantrone may be helpful.
- β interferon (1a or 1b) or pegylated β 1a, subcutaneous or intramuscular reduces number of relapse (in 30%).
- Glatiramer acetate has similar effect. It has immunomodulatory effect.
- Oral agents: Fingolimod (immunomodulator), teriflunomide (blocks proliferation of activated Lymphocytes) and dimethyl fumarate.
- Monoclonal antibody to α -integrins (natalizumab) or to lymphocyte epitopes (alemtuzumab) may be helpful in severely affected patient.
- IV immunoglobulin may be helpful in aggressive cases.

3. Supportive and symptomatic treatment for complication and disability:

- For incontinence: Intermittent self catheterization, drugs like oxybutynin, tolterodine etc.
- Urgency or frequency: Intermittent self catheterization, if post-micturition residual urine is >100 mL. If it is <100 mL, oxybutynin or tolterodine may be given.

- For spasticity: Physiotherapy and drugs like baclofen (oral or intrathecal), tizanidine, benzodiazepine or dantrolene may be used. Local intramuscular injection of botulinum toxin or chemical neuronectomy is other option. Cannabis extracts and synthetic cannabinoids are also used.
- For dysaesthesia: Carbamazepine, gabapentin, phenytoin or amitriptyline may be helpful.
- For ataxia: Isoniazid or clonazepam.
- For fatigue: Amantadine, modafinil or amitriptyline.
- For impotence: Sildenafil may be used.
- Control of infection.
- Prevention of pressure sore.
- Rehabilitation, occupational therapy, walking aids, visual aids etc.
- Counselling, patient's education.

Q: What is the **role of exercise** in MS?

A: Exercise should be avoided in active disease, may be done during remission.

N.B.: Remember the following points in MS:

- Common in women of 20 to 40 years of age (rare before puberty and after 60 years, F:M = 2:1).
- It is called **disseminated sclerosis**, as it is **disseminated in time and place**.
- Patient may complain of blurring or loss of vision. Using fundoscopy nothing is seen. ('If doctor sees nothing, patient sees nothing'). This is due to **retrobulbar neuritis**.
- Peripheral nervous system is spared, only CNS involvement.
- Causes of death are renal failure and bronchopneumonia.

MULTIPLE SCLEROSIS (PRESENTING IN OTHER FORMS)

Instruction by the examiner:

- Examine the eyes of this patient.

Presentation of a Case (Case No. 1):

- There is nystagmus on lateral movement in abducting eye but failure of adduction of other eye.
- After covering the abducted eye, there is normal adduction of other eye.

My diagnosis is **Intranuclear ophthalmoplegia (also called ataxic or dissociated nystagmus)**.

Q: What is the likely **cause**?

A: Multiple sclerosis.

N.B.: For details, see in the chapter 'examination of the eye (nystagmus)'.

Q: What **else** do you want to see in this case?

A: As follows:

- Fundoscopy: to see optic neuritis (or optic atrophy).
- Talk with the patient: cerebellar speech (also other signs of cerebellar lesion).
- Neurological examination of lower limbs: spastic paraplegia.
- Neurological examination of upper limbs: may be signs of UMN lesion one or other limb, signs of cerebellar lesions (such as dysdiadochokinesis, intention tremor, impaired finger nose pointing test). Also, signs of dorsal column lesion (such as loss of vibration and position sense). When the eyes are closed, there is involuntary writhing of fingers (pseudoathetosis).

Instruction by the examiner:

- Examine for cerebellar signs of this patient.

Presentation of a Case (Case No. 2):

- Present the case as cerebellar lesion (see later in this chapter).

My diagnosis is **Cerebellar lesion**, which may be due to multiple sclerosis.

Instruction by the examiner:

- Examine the lower limbs and talk with the patient.

Presentation of a Case (Case No. 3):

- There is spastic paraplegia with scanning (cerebellar) speech.
- No sensory loss but there is loss of vibration and position sense (dorsal column lesion).

My diagnosis is **Multiple sclerosis**.

Q: Why multiple sclerosis?

A: Because, the patient has spastic paraplegia with signs of dorsal column lesion with cerebellar speech. So, the most likely diagnosis is multiple sclerosis.

Q: What **else** do you like to see?

A: I want to examine the eye to see nystagmus, also fundoscopy to see optic neuritis or atrophy.

N.B.: Remember the following points:

- There may be different presentations of multiple sclerosis.
- Short case may be related to examination of the lower limb, eye, cerebellar signs, fundoscopy or whole neurological examination etc.
- Also, there may be examination of the gait as a short case (cerebellar or drunken or reeling gait).

TRANSVERSE MYELITIS (PRESENTING AS SPASTIC PARAPLEGIA)

Instruction by the examiner:

- Perform neurological examination of lower limbs.

Presentation of a Case: Presents as described in spastic paraplegia.

My diagnosis is **Spastic paraplegia** for which, I have some differential diagnosis (see as in spastic paraplegia).

Q: Why it is Transverse Myelitis (TM)?

A: Because, there is spastic paraplegia with definite sensory level and sphincter disturbance (the patient is on urinary catheter). All are highly suggestive of TM.

Q: Can all there flexes be diminished or absent in TM?

A: All reflexes may be diminished or absent in early stage (stage of spinal shock).

Q: What history do you like to take in TM?

A: I want to take history of:

- Onset of symptoms (usually sudden onset). The patient usually presents with fever, backache and weakness of lower limbs. Bladder involvement is an early feature.
- Upper respiratory tract infection.
- Other viral infection.
- Vaccination.
- Trauma.
- Any surgery.
- Radiotherapy (radiation myelopathy).
- History of any previous disease (such as multiple sclerosis, vasculitis, sarcoidosis, SLE).

READ THE FOLLOWING TOPICS IN RELATION TO TRANSVERSE MYELITIS

Q: What is transverse myelitis?

A: Transverse myelitis is an acute inflammatory, demyelinating disorder of spinal cord causing paraparesis or paraplegia or sometimes quadriplegia. Commonly due to post-infectious or post-vaccinal inflammation. It is the common cause of non-compressive spinal cord syndrome (or spastic paraplegia).

Typically, one or two spinal segments are affected with part or all of the cord area at that level involved (transverse means involvement of whole cross-section of spinal cord at the affected level), resulting in bilateral motor, sensory and sphincter deficit below the level of lesion.

Q: What is the common Site?

A: Mid thoracic region.

Q: What are the causes of TM?**A:** As follows:

1. Para-infectious autoimmune inflammatory response: Common cause. May follow viral infection or immunization.
2. Post-infectious inflammation:
 - Viral: coxsackie, polio, EBV, herpes virus, HIV, HTLV-1,2, HAV, influenza, echo virus.
 - Bacterial: pyogenic, tuberculous, syphilitic (rare), mycoplasma, Lyme disease.
 - Others: parasitic, fungal, schistosomiasis.
3. Traumatic.
4. Vascular (arteritis).
5. Anterior spinal artery occlusion.
6. Nutritional myelopathy.
7. Collagen vascular disease (SLE, Sjögren's syndrome, MCTD).
8. Multiple sclerosis.
9. Neuromyelitis optica.
10. ADEM.
11. Sarcoidosis.
12. Idiopathic.

Q: What are the clinical features?**A:** Usually follows viral illness or vaccination.**Symptoms:**

- Fever may be present.
- Acute or subacute onset of paralysis or paraparesis associated with back pain.
- At the level of lesion: girdle constriction with hyperaesthesia just above the lesion may be present.
- Usually no root pain, spinal tenderness or spinal deformity.
- Urinary problem like retention, incontinence as bladder involvement is early.

Signs:**Motor system:**

- Muscle tone: increased.
- Muscle power: may be diminished.
- Reflexes: exaggerated.
- Co-ordination: may be normal.
- Plantar: bilateral extensor.

Sensory: Partial or complete sensory loss with a definite upper level.**Q: What investigation should be done?****A:** As follows:

- CBC (leucocytosis in systemic infection).
- X-ray of dorsolumbar spine (to exclude other cause).
- CSF study (high protein and lymphocyte).
- MRI spinal cord with contrast (shows cord swelling and oedema with gadolinium enhancement at affected levels).
- MRI of brain (to see any demyelination).
- Other investigation according to history and suspicion of cause.

Q: How to treat?**A:** As follows:

1. General measures:
 - Reassurance and psychological support.
 - Care of bowel, bladder (catheterization), eyes, skin.
 - Passive physiotherapy.
 - For spasticity: baclofen, diazepam, tizanidine.
 - Rehabilitation.
2. Treatment of specific cause, if any.
3. In patient with severe and rapidly progressive disease: high dose IV methylprednisolone (1 gm IV with 5% DA 200 cc in 1 hour for 3 to 5 days).
4. Anti-viral (IV acyclovir), antibiotic (in bacterial infection) or anti-parasitic.
5. Plasmapheresis (if no response to steroid).

Q: What is the prognosis?**A:** Recovery occurs over a period of weeks or months.

- 1/3rd have static deficit.
- 1/3rd go on to develop multiple sclerosis.
- 1/3rd recover with no subsequent relapse.

Q: What are the factors associated with increased or decreased risk of developing multiple sclerosis after TM?**A:** As follows:

Increased Risk	Decreased Risk
• Severe weakness • Catastrophic onset • Initial lancinating pain • Sensory disturbance at cervical level • Spinal shock • Incontinence • Presence of 14-3-3 protein in CSF	• Subacute onset over days • Young onset • Retained posterior column function • Retained tendon reflexes • Early recovery

FLACCID PARAPLEGIA

Common cases in flaccid paraplegia are Guillain–Barré syndrome (GBS) and peripheral neuropathy.

Instruction by the examiner:

- Examine the lower limbs. Or, perform the neurological examination of the lower limbs.

Presentation of a Case:

- There is wasting of muscles in both lower limbs (mention, up to where) with hypotonia.
- Muscle power is diminished, grade 2/5 (mention where).
- Both knee and ankle jerks: Diminished or absent (ensure that you have done reinforcement).
- Plantar: Normal or equivocal on both sides.
- There is no sensory abnormality (may be some sensory abnormality, mention if any).
- Vibration and position senses are normal.
- Coordination: Could not be elicited due to weakness.
- Gait: Unable to walk due to weakness.

My diagnosis is **Flaccid paraplegia**.

Q: What is the **more likely** diagnosis?

A: May be due to GBS.

Q: What are the **causes** of flaccid paraplegia?

A: As follows:

- GBS.
- Motor neuropathy due to any cause.
- Tabes dorsalis.
- Friedreich's ataxia.
- Progressive muscular atrophy (one type of MND).
- Acute inflammatory demyelinating polyradiculopathy (AIDP).
- Hysterical conversion reaction (HCR).

Q: What are the **causes** of **predominant motor neuropathy**?

A: As follows:

- GBS.
- Charcot–Marie–Tooth disease.
- Acute intermittent porphyria.
- Chronic lead poisoning.
- Diabetic amyotrophy.
- Diphtheria.
- Paraneoplastic syndrome.

Q: Can it be Friedrich's ataxia?

A: Unlikely. Because, in Friedrich's ataxia, following features should be present:

- It usually occurs in early age.
- Signs of posterior column lesion (loss of vibration and position sense).
- Signs of cerebellar lesion.
- Pes cavus and kyphosis may be present.
- Loss of knee and ankle jerk, plantar is extensor.

Q: Can it be SCD?

A: Unlikely. As, in SCD, there should be features of:

- Peripheral neuropathy.
- Dorsal column lesion.
- Pyramidal lesion (loss of knee and ankle jerk, but plantar is extensor).

Q: What investigation do you suggest in flaccid paraplegia?

A: Investigation should be done according to suspicion of cause.

GUILLAIN-BARRÉ SYNDROME (PRESENTING AS FLACCID PARAPLEGIA)

Instruction by the examiner:

- Examine the lower limbs. Or, perform the neurological examination of the lower limbs.

Presentation of a Case: Present as above.

My diagnosis is **Flaccid paraplegia**, more likely GBS.

Q: Why GBS?

A: Because, there is LMN lesion involving both lower limbs with no sensory loss.

Q: What are the other possible differential diagnoses?

A: As follows:

Spinal cord compression (in stage of spinal shock), hypo or hyperkalaemia, myasthenia gravis, chronic inflammatory demyelinating polyneuropathy, botulism, paraneoplastic neuropathy.

Q: Can it be transverse myelitis?

A: As follows:

Unlikely. As in transverse Myelitis, there is spastic paraplegia with definite sensory level and sphincter disturbance (the patient is on urinary catheter).

Q: If it is GBS, what else do you want to examine?

A: As follows:

- In the upper limb: Both may show features of flaccid weakness (all four limbs may be paralyzed at the same time).
- Loss of all reflexes (an important clue).
- Cranial nerve: Bilateral facial palsy may occur.
- Fundoscopy: Papilloedema may be present.

Q: How does the patient of GBS usually present?

A: As follows:

- History of upper respiratory tract infection (URTI) or gastroenteritis (viral or bacterial).
- After 1 to 3 weeks, there may be distal paraesthesia and pain followed by weakness of lower limbs that ascends over several weeks (ascending paralysis). It may advance quickly thereby affecting all the limbs at once and can lead to paralysis (quadriplegia).
- Respiratory paralysis in 20% case. Progressive respiratory involvement and paralysis is the main problem.
- Paraesthesia and pain in back and limbs may occur.
- Facial and bulbar weakness.
- Autonomic dysfunction: Change of blood pressure, tachycardia, increased sweating, dysrhythmia may occur.

Brief clinical findings in GBS:

- Flaccid paralysis involving lower limbs and may involve all four limbs.
- Loss of all reflexes.
- Bilateral facial palsy in 50% cases, unilateral facial palsy in 25% cases.
- Sensory loss: Minimum or absent.
- Sphincter involvement (rare).

N.B.: Remember the following points:

- Diffuse weakness with loss of all reflexes: A very striking finding in GBS.
- GBS may be associated with Hodgkin's lymphoma.
- Papilloedema may develop.
- Syndrome of inappropriate antidiuretic hormone (SIADH) may develop.

Q: What are the dangerous complications of GBS (cause of death)?

A: As follows:

- Respiratory muscle paralysis. The patient may develop respiratory failure within hours.
- Bulbar palsy (manifested as dysphagia, nasal regurgitation).
- Cardiac conduction block.
- Cardiac arrhythmia.

Q: What is GBS?

A: It is a post-infective demyelinating neuropathy of unknown cause, usually 1 to 3 weeks after respiratory infection, diarrhoea and occasionally after vaccination or surgery. There is demyelination of peripheral nerve or spinal root, which is immunologically mediated. This may follow after infection with cytomegalovirus or *Mycoplasma* or *Campylobacter jejuni*. GBS is mono-phasic and does not recur.

Q: What is the cause of GBS? What is the mechanism?

A: GBS develops 1 to 3 weeks after respiratory infection or diarrhoea (mainly by *Campylobacter*) in 70% cases. Triggering factors may be *Campylobacter jejuni*, cytomegalovirus, *Mycoplasma*, herpes zoster, HIV, Epstein–Barr virus infection.

2 mechanisms are involved:

1. Demyelinating: Acute inflammatory demyelinating polyneuropathy (AIDP).
2. Axonal, which may be:
 - Motor: Acute motor axonal neuropathy (AMAN).
 - Sensorimotor: Acute motor and sensory axonal neuropathy (AMSAN).

Q: What investigations do you suggest in GBS?

A: As follows:

- Lumbar puncture and CSF analysis: Typical finding is 'albumino-cytological dissociation' (albumin may be very high, >1000 mg%, lymphocytes are slightly raised or normal, <20/mm³. If lymphocyte is >50, GBS is unlikely. CSF protein may be normal in first 10 days).
- Frequent monitoring of respiratory function tests (forced vital capacity, FEV₁, peak expiratory flow rate).
- Arterial blood gas analysis (as respiratory failure may occur at any time).
- Nerve conduction study (shows slow conduction or conduction block. Demyelinating neuropathy found after 1 week).
- Investigation to identify CMV, *Mycoplasma* or *Campylobacter* should be done.
- Serum electrolytes (to exclude hypo or hyperkalaemia).

Note: Triad of acute symmetrical ascending paralysis of limbs are flexia and albumin-cytological dissociation in CSF is highly suggestive of GBS.

Q: What is Miller–Fisher syndrome?

A: It is a variant of GBS characterized by triad of ophthalmoplegia, ataxia and are flexia. It is a rare disease. Antibodies against GQ1b (ganglioside) have a sensitivity of 90%.

Q: How to treat GBS?

A: As follows:

- Ideally the patient should be treated in ICU and respiratory function should be monitored regularly (vital capacity and arterial blood gases). The patient may require artificial ventilation.
- High dose intravenous immunoglobulin should be given to all patients (it reduces the duration and severity). Dose is 400 mg/kg/day for 5 days. It is helpful, if given within 14 days. It may precipitate angina or myocardial infarction. In congenital IgA deficiency, it may cause allergic reaction.
- Plasma exchange if given within 14 days is equally effective in reducing the severity and duration of GBS.
- Steroid has no proven value (may worsen).
- Methylprednisolone with immunoglobulin has no proven benefit.
- Plasmapheresis may be required.
- Physiotherapy is the mainstay of therapy.
- Prevention of pressure sore and venous thrombosis.
- Other symptomatic treatment.

Q: What are the indication of ventilation?

A: As follows:

1. Impending respiratory failure:
 - Tachypnoea.
 - Decrease in arterial O₂ tension <85 mmHg.
 - Forced vital capacity (FVC) <20 mL/kg.
 - Maximum inspiratory pressure <30 cm H₂O.
 - Maximum expiratory pressure <40 cm H₂O.
2. FVC <1.5 L.
3. PaO₂ <10 kPa.
4. PaCO₂ >6 kPa.
5. Rapid progression of disease.
6. Bulbar dysfunction.
7. Bilateral facial palsy.
8. Autonomic involvement.

Q: What is the prognosis of GBS?

A: As follows:

- 80% recovery, may take several months (3 to 6 months). If axons have been damaged, regeneration may require 6 to 18 months or longer.
- 10% residual disability (may be up to 30%).
- 3 to 5% die (in some study, up to 10% deaths).

Q: What are the bad and good **prognostic factors**?

A: As follows:

Adverse prognostic factors:

- Preceding GI infection.
- >60 years of age.
- Severe or rapidly evolving form of the disease (maximum disability within 7 days).
- Descending paralysis.
- Bulbar weakness.
- Autonomic dysfunction.
- Asymmetrical weakness.
- Very high CSF protein.
- Evidence of widespread axonal damage.
- Those requiring early and prolonged mechanical ventilatory assistance.

Good prognostic factors:

- Young age.
- Preceding H/O respiratory infection.
- Symmetrical involvement.
- Slowly progressive.
- Facial nerve involvement.
- Demyelinating disease.
- No respiratory involvement.
- Ascending paralysis.
- Early treatment.
- Early recovery.

MONOPLÉGIA (BROWN–SÉQUARD SYNDROME)

Instruction by the examiner:

- Examine the lower limbs. Or perform the neurological examination of the lower limbs.

Presentation of a Case (Supposing Right Lower Limb):

- There is hypertonia and weakness of extensors and flexors of knee and ankle.
- Knee and ankle jerks are exaggerated, plantar is extensor.
- No sensory impairment, but loss of vibration and joint position sense.
- In the left lower limb: Loss of pain and temperature extending up to just below umbilicus (T_{8,9}), but vibration and joint position sense and light touch are intact.

My diagnosis is **Hemisection of spinal cord in the right side (Brown–Séquad syndrome)**.

Q: What is **Brown–Séquad syndrome**? What are the **causes**?

A: It is due to the damage on one side or hemisection of the spinal cord characterized by:

1. On the side of lesion:
 - At the level: Band of hyperaesthesia and LMN lesion.
 - Below the level: Loss of vibration and position sense (posterior column) and UMN lesion.
2. Contralateral (opposite) side: Loss of pain and temperature (spinothalamic tract lesion) below the level of lesion, giving rise to dissociated sensory loss.

Q: What are the **causes of Brown–Séquad syndrome**?

A: AS follows:

- Compression of spinal cord tumour (glioma or angioma).
- Multiple sclerosis.
- Myelitis.
- Trauma.
- Radiation myelopathy.

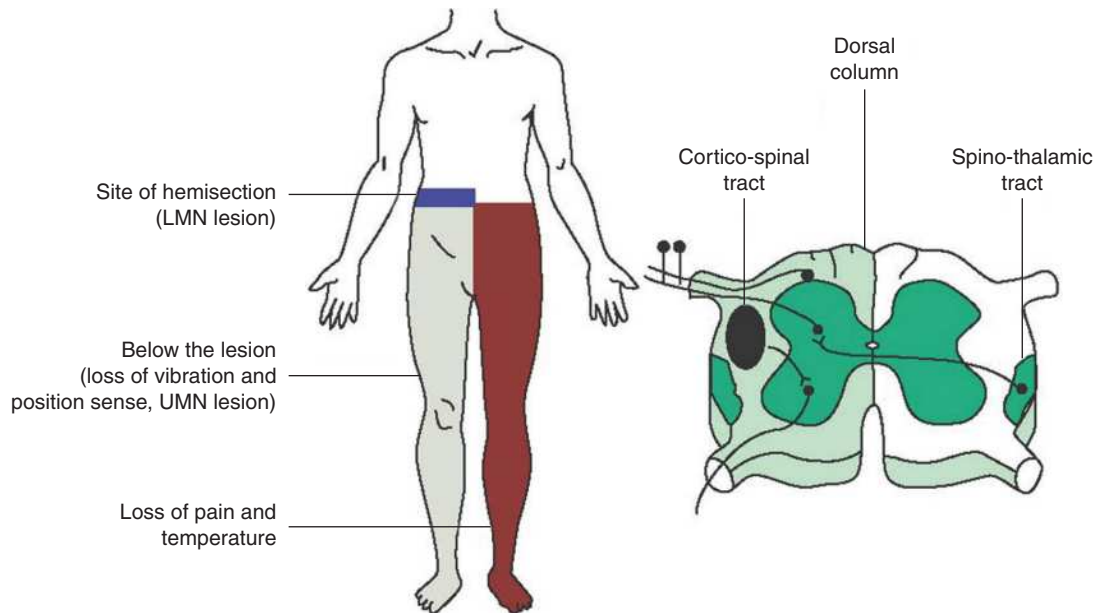
The patient complains of numbness of one side, whereas weakness, heaviness and stiffness on other sides.

N.B.: If lesion is high up (C_{5,6}), there may be hemiplegia.

Q: What investigations should be done?

A: As follows:

- MRI of spinal cord.
- Others: According to suspicion of cause, e.g., CSF study, viral serology, vitamin B₁₂ level, syphilitic serology (if any).



OLD POLIOMYELITIS (PRESENTING AS MONOPLÉGIA)

Instruction by the examiner:

- Perform neurological examination of lower limbs.

Presentation of a Case (Supposing Right Side):

- Right lower limb is short and pes cavus is present.
- There is wasting of muscles with hypotonia.
- Muscle power is diminished, grade 3/5.
- Knee and ankle jerks: Diminished (or absent), plantar is normal (or equivocal).
- No sensory abnormality, vibration and position senses are normal.
- Co-ordination: Impaired.

My diagnosis is **Monoplegia of the right lower limb**.

Q: What are the causes?

A: As follows:

- Old poliomyelitis.
- Hemiatrophy.

Q: What is the site of lesion in this case?

A: Anterior horn cell of the spinal cord (commonly in lumbar region).

Q: What is the site of lesion of weakness of one limb or monoplegia?

A: Brachial plexus (upper limb), lumbosacral plexus (lower limb) and central lesion (in motor cortex or partial internal capsule).

Q: What are the sites affected by polio virus?

A: Spinal cord (anterior horn cell), brainstem, cerebral cortex and motor cranial nerve nuclei.

Q: What is the sensory abnormality in poliomyelitis?

A: Usually, no sensory abnormality.

Q: What is the typical finding in poliomyelitis?

A: Asymmetrical flaccid paralysis with no sensory loss.

Q: What is the cause of poliomyelitis?

A: It is caused by polio virus, an enterovirus in picornaviridae family. It is of 3 types:

- Type I: Brunhilde (commonest type, 80% of paralytic illness).
- Type II: Lansing.
- Type III: Leon.

Q: What are the types of vaccine for polio myelitis?

A: 2 types:

- Oral live attenuated polio virus (OPV) or Sabin vaccine.
- Inactivated polio virus (IPV) or Salk vaccine (less used because OPV is cheaper and easily administered).



Hemiatrophy



Poliomyelitis

Q: What is the **complication** of OPV (also called provocation poliomyelitis)?

A: It can cause vaccine associated paralytic poliomyelitis (VAPP) in a small percentage of recipients, particularly in immunodeficient patient. In such cases, individuals and their family members should take IPV.

Q: What is **provocation poliomyelitis**?

A: It is caused by administration of IM injection during the incubation period of wild poliovirus or shortly after exposure of OPV.

Q: What are the **types** of poliomyelitis?

A: 4 types:

- Abortive: Characterized by fever, myalgia, sore throat etc. Self-limiting.
- Non-paralytic: Above features plus signs of meningeal irritation. Complete recovery occurs.
- Paralytic: Above features that subside in 4 to 5 days, may recur with signs of meningeal irritation, muscular pain followed by asymmetric flaccid paralysis.
- Bulbar polio: Characterized by cranial nerve involvement and respiratory muscle paralysis. Also, soft palate, pharyngeal and laryngeal muscle paralysis is common.

POLYNEUROPATHY

Instruction by the examiner:

- Perform neurological examination of lower limbs or upper limbs.

Presentation of Case No. 1:

- Skin is shiny, dry with loss of hair, ulcer and callosities present on the sole of foot.
- Wasting of muscles of feet and legs are present.
- Muscle tone and power are diminished.
- All the reflexes are diminished or absent.
- There is bilateral symmetrical sensory loss in stocking pattern with light touch and pin prick (mention up to where) and also loss of vibration and position senses.
- Co-ordination: could not be done due to weakness.
- Gait is ataxic with wide based and high steppage.
- Rombergism is positive.

My diagnosis is **Peripheral neuropathy (mixed motor and sensory type)**.

Q: What is the **presentation** of peripheral neuropathy?

A: Weakness, difficulty in walking, tingling, numbness, heaviness of limbs.

Q: Can it be **GBS**?

A: Less likely or unlikely, as in GBS, there is usually motor neuropathy. No sensory neuropathy (may occur rarely).

Q: What do you think is the **cause** in this case?

A: As follows (mention according to the age of the patient):

- Diabetes mellitus.
- Alcoholism.
- Nutritional deficiency (B₁, B₆, B₁₂, folic acid, pantothenic acid and vitamin E).
- Malignancy, e.g., bronchial carcinoma (in elderly).
- Drugs (isoniazid, vincristine, phenytoin, amiodarone, statins, cisplatin, dapsone).
- Infections (e.g., leprosy).
- Idiopathic.

Q: Could it be **MND**?

A: No. In MND, there is no sensory loss (fasciculation is present).

Q: What are the **causes** of **predominantly sensory neuropathy**?

A: As follows:

- Diabetes mellitus.
- Alcoholism.
- Infection: Leprosy, HIV, Lyme disease.
- Deficiency of vitamins B₁, B₆ and B₁₂.
- Chronic kidney disease.
- Hypothyroidism.
- Paraneoplastic neuropathy (e.g., bronchial carcinoma).
- Drugs (INH, vincristine, metronidazole, chloroquine, pyridoxine, colchicine).
- Hereditary sensory neuropathy.
- Multiple myeloma.

Presentation of Case No. 2:

- There is wasting of all the muscles of lower limbs.
- Muscle power is diminished, grades 3/5 and 4/5.
- Muscle tone is also diminished.
- Knee and ankle jerks are diminished (or absent), plantar response is equivocal.
- All modalities of sensation are normal.

My diagnosis is **Peripheral neuropathy (predominantly motor type)**.

Q: What is the **presentation** of motor neuropathy?

A: Weakness, difficulty in walking, heaviness of limbs, difficulty in standing from sitting. If upper limbs are involved, difficulty in raising the limbs above the head.

Q: What are the **causes** of **predominantly motor neuropathy**?

A: As follows:

- Guillain–Barré syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP).
- Charcot–Marie–Tooth disease.
- Acute intermittent porphyria.
- Chronic lead poisoning.
- Diabetic amyotrophy.
- Diphtheria.
- Drug (dapsone).
- Paraneoplastic syndrome.
- POEMS (**P**eripheral neuropathy, **O**rganomegaly, **E**ndocrinopathy, **M**-protein, **S**kin changes).

Presentation of Case No. 3: Upper Limb

- There is wasting of the small muscles of hands, extending up to the middle part of both forearms.
- All the small muscles of hands are weak.
- Muscles of forearm and arm are also weak.
- Muscle tone is diminished.
- All the reflexes are diminished or absent.
- There is bilateral symmetrical sensory loss in gloves pattern with light touch and pin prick (mention up to where).

My diagnosis is **Peripheral neuropathy (mixed type)**.

Q: What **else** do you want to examine in this case?

A: I want to examine the lower limbs to see any evidence of neuropathy.

Q: What is the **difference** between small and large fibre neuropathy?

A: As follows:

- In small fibre neuropathy, A δ and unmyelinated C fibres are affected. Touch, pressure, vibration and joint position senses are intact. Pain and temperature sensation are lost. There is autonomic dysfunction.
- In large fibre neuropathy, there is loss of touch, pressure, vibration and joint position sense (sensory ataxia). Pain and temperature sensation are preserved.

READ THE FOLLOWING TOPICS IN RELATION TO POLYNEUROPATHY

Q: What are the **causes** of peripheral neuropathy (theoretically)?

A: As follows:

- Diabetes mellitus.
- Nutritional deficiency (B₁, B₆, B₁₂, folic acid, pantothenic acid and vitamin E).
- Malignancy (bronchial carcinoma, lymphoma and multiple myeloma).
- Drugs (isoniazid, vincristine, phenytoin, amiodarone, statins, cisplatin and dapsone).
- Alcoholism.
- Guillain–Barré syndrome.
- Infections (leprosy, HIV, typhoid and diphtheria).
- Collagen disease (SLE, polyarteritis nodosa, rheumatoid arthritis).
- CKD.
- Chronic inflammatory demyelinating polyneuropathy (CIDP).
- Idiopathic (in many cases).

Q: What are the **mechanisms** of neuropathy?

A: As follows:

- Demyelination.
- Axonal degeneration.
- Wallerian degeneration (after section of nerve, there is axonal and myelin sheath degeneration).
- Compression (called entrapment neuropathy), there is segmental degeneration at the site of compression.
- Infarction of nerve: *microinfarction* of nerve due to arteritis of vessels supplying the nerve (found in diabetes mellitus, polyarteritis nodosa).
- Infiltration in nerve (found in leprosy, sarcoidosis, malignancy).

Q: What are the **causes** of **painful neuropathy**?

A: As follows:

- Diabetes mellitus.
- Deficiency of vitamins B₁ and B₁₂.
- Alcohol.
- Carcinomatous neuropathy.
- Porphyria.
- Arsenic poisoning.

Q: How to **treat** painful neuropathy?

A: Tricyclic antidepressant, phenytoin, carbamazepine and topical capsaicin.

Q: How to **differentiate** between demyelination and axonal degeneration?

A: By NCS and electromyography (EMG):

- In demyelination: there is slowing of nerve conduction, amplitude of nerve action potential (CMAP) is normal.
- In axonal degeneration: conduction velocity is normal as axonal continuity is maintained in surviving fibres, amplitude of CMAP is reduced. Using needle EMG, denervation on the affected muscles may be demonstrated.

Q: Which part is first involved in peripheral neuropathy? Why?

A: Usually distal part of the limbs is commonly involved, because longer the nerve fibre earlier is the involvement. Since the nerve fibres supplying the distal parts of the limbs are longer, they are first affected.

Q: What are the causes of demyelination and axonal degeneration?

A: As follows:

1. Causes of demyelination:
 - Guillain–Barré syndrome.
 - Chronic inflammatory demyelinating *polyradiculoneuropathy*.
 - Hereditary sensory motor neuropathy.
 - Charcot–Marie–Tooth disease type 1 and type X.
 - Paraprotein-associated demyelinating neuropathy.
 - Multifocal motor neuropathy.
 - Vitamin B₁₂ deficiency.
 - Diphtheria.
 - Refsum’s disease.
 - HIV.
2. Causes of axonal degeneration:
 - Toxic neuropathy (alcohol and drugs).
 - Diabetes mellitus.
 - Paraneoplastic.
 - IgG paraproteinaemia.
 - Hereditary.
 - Vitamin deficiency.
 - Idiopathic.

Q: What are the types of neuropathy in DM?

A: As follows:

- Sensory neuropathy (common).
- Mixed motor and sensory neuropathy.
- Asymmetrical motor neuropathy (diabetic amyotrophy).
- Autonomic neuropathy.
- Mononeuropathy.
- Mononeuritis multiplex.

Q: What is the mechanism of neuropathy in DM?

A: As follows:

- Axonal degeneration.
- Patchy or segmental demyelination.
- Involvement of intraneural capillaries.

Q: What are the causes of autonomic neuropathy?

A: As follows:

- Diabetes mellitus.
- Guillain–Barré syndrome.
- Paraneoplastic.
- Amyloidosis.
- Shy dragger syndrome (Multiple system atrophy).
- HIV.

Q: What is **mononeuritis multiplex** and what are the **causes**?

A: Separate involvement of more than one peripheral nerve or cranial nerve by a single disease is called mononeuritis multiplex. It is due to involvement of vasa *nervorum* or malignant infiltration of nerves. **Causes** are:

- Diabetes mellitus.
- Leprosy.
- Rheumatoid arthritis.
- Vasculitis (SLE, polyarteritis nodosa).
- Amyloidosis.
- Malignancy (carcinomatous neuropathy).
- Sarcoidosis.
- Lymphoma.
- HIV, Hepatitis C infection.
- Wegener granulomatosis.
- Acromegaly.
- Paraproteinaemia.
- Lyme disease.
- Idiopathic multifocal motor neuropathy.

Causes of **acute mononeuritis multiplex** (usually vascular):

- Polyarteritis nodosa.
- Diabetes mellitus.
- Collagen disease (SLE, RA).

Q: What **investigations** should be done in polyneuropathy?

A: As follows:

- CBC with PBF (macrocytosis in megaloblastic anaemia with subacute combined degeneration).
- CRP.
- Blood sugar.
- Chest X-ray (to exclude bronchial carcinoma).
- Serum B₁₂ and folate assay.
- Renal and hepatic function.
- Bone marrow (megaloblast in SCD).
- Nerve conduction study (to see axonal or demyelinating).
- Other investigations according to suspicion of causes (such as ANA, RA, ANCA).

Q: What are the **causes** of thickening of nerves?

A: As follows:

- Leprosy.
- Neurofibroma.
- Amyloidosis.
- Acromegaly.
- Sarcoidosis.
- Charcot–Marie–Tooth disease (hereditary motor and sensory neuropathy).
- Repeated friction or trauma.
- Refsum disease.
- Dejerine–Sottas disease (hypertrophic peripheral neuropathy).

SUBACUTE COMBINED DEGENERATION (PRESENTING AS POLYNEUROPATHY)

Instruction by the examiner:

- Perform neurological examination of lower limbs.

Presentation of a Case:

- There is wasting of all the muscles of lower limbs.
- Muscle power is diminished, grades 3/5 and 4/5.
- Muscle tone is also diminished.
- Knee jerk is brisk (ankle jerk is lost or absent) and planter is extensor.
- All modalities of sensation are lost, vibration and position sense are also lost.
- Co-ordination: could not be tested because of weakness.
- Gait: High steppage or stomping gait (sensory ataxia).
- Rombergism is positive.

My diagnosis is **Peripheral neuropathy**.

Q: What do you think is the **cause** in this case and why?

A: I think this is a case of **SCD**, because there are:

- Peripheral neuropathy.
- Signs of posterior column lesion (loss of vibration and position sense).
- Signs of pyramidal lesion (plantar is extensor, knee jerk is brisk and ankle jerk is absent).
- Rombergism is positive.

Q: What **else** do you want to see, if it is SCD?

A: As follows:

- Anaemia (may be lemon yellow pallor in pernicious anaemia).
- Glossitis (smooth tongue).
- Examination of abdomen may show: Mass of carcinoma stomach or scar mark in the abdomen (if gastrectomy).
- Fundoscopy of eye shows optic atrophy.
- Evidence of dementia.

***N.B.:** Anaemia is usually present, but sometimes vitamin B₁₂ neuropathy may not be associated with anaemia and there may be normal blood picture with normal marrow. Serum B₁₂ should be measured.*

Q: What **history** do you like to take in SCD?

A: As follows:

- Family history of pernicious anaemia (intrinsic factor deficiency).
- History of gastrectomy (intrinsic factor deficiency), resection of ileum (impaired vitamin B₁₂ absorption).
- Frequent diarrhoea (due to Crohn's disease).
- Patient's dietary habit (if the patient is vegetarian).
- History of chronic pancreatitis.
- History of infection with *Diphyllobothrium latum*.

Q: Why it is called **combined degeneration**? (Or, what is the lesion in SCD?)

A: Because there are:

- Posterior column lesion (degeneration of ascending tract of posterior column).
- Pyramidal lesion (degeneration of descending pyramidal tracts in lateral column).
- Demyelination of peripheral nerve (peripheral neuropathy).

Q: What are the **presentations** of SCD?

A: The patient usually complains of tingling or numbness, or burning sensation and weakness in the limbs. Features of anaemia due to B₁₂ deficiency.

Q: Why **polyneuropathy** in SCD?

A: It is due to demyelination.

Q: What is the **type of anaemia** in SCD?

A: Macrocytic (megaloblastic) anaemia due to vitamin B₁₂ deficiency.

Q: What **happens** if blood transfusion is given in vitamin B₁₂ neuropathy with severe anaemia?

A: Blood transfusion or packed cell should be avoided without correcting vitamin B₁₂, otherwise neurological manifestation may be aggravated.

Q: What is the **daily requirement** of vitamin B₁₂? **How long** does it take to develop deficiency of vitamin B₁₂?

A: 1 to 2 mg daily. To develop deficiency, it takes about 3 years.

Q: What are the **causes of** vitamin B₁₂ deficiency?

A: As follows:

- Addisonian pernicious anaemia.
- Total gastrectomy (B₁₂ injection should be given every 3 months) or partial gastrectomy (10 to 20% develop B₁₂ deficiency within 5 years, B₁₂ injection should be given every year).
- Ileal disease (Crohn's disease, ileal resection).
- Stagnant loop syndrome.
- Pancreatic insufficiency (due to failure to transfer vitamin B₁₂ from R-protein to intrinsic factor).
- Vegetarian diet.
- Chronic tropical sprue.
- Fish tapeworm (*D. latum*).
- Congenital intrinsic factor deficiency.

READ THE FOLLOWING TOPICS IN RELATION TO SCD

Q: What is SCD?

A: It is a clinical syndrome due to vitamin B₁₂ deficiency, in which there is degeneration of dorsal and lateral column of spinal cord with demyelination of peripheral nerves.

Q: What are the clinical features of SCD?**A:** As follows:

- Age: 40 to 60 years, equal sex involvement.
- Sensory symptoms: Paraesthesia, tingling or numbness, starting in toes and fingers. Lower limbs are more commonly affected than the upper limbs.
- Motor symptoms: Weakness, ataxia and loss of all reflexes. May be exaggerated knee reflex with loss of ankle jerk, but extensor plantar.
- Bladder involvement: Urinary incontinence and dribbling, usually in late stage.
- Eye: Optic atrophy.
- Glossitis in the tongue. Lemon-yellow pallor (in pernicious anaemia).
- Mental change: Dementia, impaired memory, confusion and depression.

Q: What investigations are done in SCD?**A:** As follows:

1. CBC and PBF (macrocytosis and hypersegmented neutrophil).
2. Bone marrow (to see megaloblast).
3. Serum B₁₂ assay.
4. Other investigations according to the suspicion of cause:
 - For Addisonian pernicious anaemia: Anti-parietal cell and anti-intrinsic factor antibody, endoscopy and biopsy to see gastric atrophy.
 - Investigation for Crohn's disease, pancreatic disease.

*N.B.: Macrocytosis in blood and megaloblastic marrow are invariable in SCD.***Q: How to treat SCD?****A:** As follows:

- Injection vitamin B₁₂: 1000 µgm IM, 5 doses, 2 to 3 days apart and then every 3 months, to be continued for lifelong (specially in Addisonian pernicious anaemia).
- Following B₁₂ therapy, iron deficiency may occur in the first few weeks. So, oral iron therapy should be given.
- Also, following therapy there may be hypokalaemia, which may need correction.
- B₁₂ orally 2 mg/day may be given. 1 to 2% is absorbed by diffusion without intrinsic factor.
- Sublingual B₁₂ may be effective.
- Treatment of primary cause.

Q: What precaution should be taken in combined folate and vitamin B₁₂ deficiency?**A:** If folic acid deficiency is present with vitamin B₁₂ deficiency, only folic acid replacement should not be given without B₁₂. Otherwise, neurological features may deteriorate.**Q: Will you transfuse blood in this patient?****A:** Blood transfusion is avoided as it may precipitate heart failure. Also, before replacing B₁₂, if blood transfusion or packed cell is given, it may aggravate neurological manifestations. However, blood (or packed cell) transfusion may be considered if there is:

- Angina.
- Heart failure.
- Cerebral hypoxia (confusion, dizziness etc.).

Q: How to see the **response**?

A: Clinical improvement may occur within 48 hours, reticulocytosis may be seen after 2 to 3 days of starting therapy. Haemoglobin level rises by 1 g/dL every week.

Q: What is the **response** of neurological lesion to vitamin B₁₂ therapy?

A: Response is variable.

- It may improve, remain unchanged or may even deteriorate.
- Sensory abnormalities improve more than motor and peripheral neuropathy responses, better than myelopathy.
- Sensory neuropathy takes 6 to 12 months for recovery, longstanding polyneuropathy may not be improved.

Q: What are the **causes** of posterior or dorsal column lesion?

A: As follows:

- Subacute combined degeneration.
- Tabes dorsalis.
- Friedreich's ataxia.
- Multiple sclerosis.
- Brown–Séquard syndrome (ipsilateral leg).

***N.B.:** Neurological features of vitamin B₁₂ deficiency should be excluded in any patient with any of the following unexplained diseases:*

- *Peripheral sensory neuropathy.*
- *Spinal cord disease (posterior column lesion and corticospinal tract lesion).*
- *Optic atrophy (rare).*
- *Dementia (rare).*
- *Autonomic neuropathy.*

Q: What are the **features of tabes dorsalis**?

A: As follows:

- Signs of dorsal column lesion (loss of vibration and position sense). Squeezing of the calf muscles and the Achilles tendon produces no pain (deep sensation is lost).
- Bladder involvement: Common.
- Eye signs: Argyll Robertson pupil and bilateral ptosis.
- Rombergism: Positive.

MOTOR NEURON DISEASE (MND)

Instruction by the examiner:

- Neurological examination of lower limbs or upper limbs.
- Look at the legs. What is your finding? (Fasciculation.) What else do you want to examine?
- Examine the hands (wasting).

Presentation of Case No. 1 (Lower Limb):

- There is wasting of all the muscles of lower limbs and fasciculation are present (mention the location).
- Muscle power is diminished (mention the location), grades 3/5 and 4/5 with hypertonia.
- Knee and ankle jerks are exaggerated, also patellar or ankle clonus (mention, if any).
- Plantar response: Extensor on both sides.
- Sensory is normal.
- Coordination: Difficult to elicit because of weakness.
- Gait: The patient is unable to walk (may be spastic gait).

My diagnosis is **Motor neuron disease**.

Remember, if the following finding are present, diagnosis is motor neuron disease, until proved otherwise:

- Wasting of muscles (weak also).
- But exaggerated reflex.
- No sensory loss.
- Fasciculation is present.

N.B.: During examination of a case of MND, if the patient looks emotionally upset and there is dribbling of saliva, it is suggestive of pseudobulbar palsy.

Q: What else do you like to examine?

A: As follows:

1. Upper limbs: signs of LMN lesion in the upper limb (then the diagnosis is amyotrophic lateral sclerosis).
2. Tongue:
 - Wasting and fasciculation (bulbar palsy). Then talk with the patient (nasal voice) and ask about nasal regurgitation.
 - Spastic (pseudobulbar palsy).
3. Jaw jerk (exaggerated in pseudobulbar palsy).
4. Emotionally upset (pseudobulbar palsy).

Q: What are the differential diagnoses?

A: As follows:

1. Diabetes mellitus.
2. Syphilitic amyotrophy or syphilitic cervical pachymeningitis.
3. Paraneoplastic syndrome (commonly due to bronchial carcinoma).
4. Sarcoidosis.

5. Spinal diseases:

- Cervical cord compression.
- CASHA (chronic asymmetrical spinal muscular atrophy).
- Old poliomyelitis (confuses with progressive muscular atrophy).
- Spinal muscular atrophy of juvenile-onset type-3 (onset in childhood, mild form, affects mostly proximal muscles).
- Motor neuropathy due to any cause (confuses with progressive muscular atrophy).

Q: Could it be **syringomyelia**?

A: Unlikely, as in syringomyelia, there is dissociated sensory loss.

Q: Could it be **spinal cord compression**?

A: Unlikely. As, there is sensory loss in spinal cord compression.

Presentation of Case No. 2 (Examination of Hands):

- There is generalized wasting of small muscles of hands involving thenar, hypothenar and interossei muscles with dorsal guttering and claw hand (flexion of interphalangeal joints and extension of metacarpophalangeal joints).
- Muscle power of small muscles of hand are diminished.
- There is no sensory loss.

My diagnosis is **Motor neuron disease (progressive muscular atrophy)**.

Q: What is the **point in favour** of your diagnosis?

A: LMN lesion but no sensory loss.

Q: If there is **sensory loss**, what are the likely diagnoses?

A: If there is loss of sensation, my differential diagnoses are:

- Peripheral neuropathy due to any cause.
- Cervical spondylosis.
- Cervical rib.
- Cervical cord compression (such as neurofibroma and meningioma).
- Leprosy.
- Syringomyelia (dissociated sensory loss and trophic changes in hand).

Q: What are the causes of **wasting of the small muscles of the hand**?

A: As follows:

- MND.
- Syringomyelia.
- Charcot–Marie–Tooth disease.
- Cervical spondylosis.
- Cervical rib.
- Pancoast tumour.
- Following arthritis (e.g., rheumatoid arthritis).
- Peripheral nerve lesion (peripheral neuropathy or combined ulnar and medial nerve lesion).
- Myopathy (dystrophia myotonica).



Wasting in MND



Wasting of thenar and hypothenar muscles—claw hand

N.B.: There are certain ‘No’s in MND:

- *No sphincter disturbance (rarely involved in late case).*
- *No sensory involvement.*
- *No loss of awareness till death.*
- *No dementia.*
- *No ocular muscle involvement.*
- *No cerebellar or extrapyramidal lesion.*
- *No abnormality of CSF usually.*

READ THE FOLLOWING TOPICS IN RELATION TO MND

Q: What is MND? What are the **causes** of MND?

A: It is a progressive disease of unknown cause, characterized by degeneration of motor neurons in the spinal cord, cranial nerve nuclei and pyramidal neurons in the motor cortex.

MND is common in middle aged and elderly, rare before 30 years of age. Males are commonly affected than females (pseudobulbar palsy is more in females). There is no remission and the disease is fatal within 3 to 5 years. Young patient and those with bulbar symptoms shows rapid progression.

Causes are unknown, possible factors are:

- Familial: 5 to 10% cases, may be inherited as autosomal dominant.
- May follow viral infection, trauma, exposure to toxin and electric shock.
- Glutamate toxicity has been implicated as a factor in amyotrophic lateral sclerosis.

Q: What is the pathology of MND?

A: Degeneration of Betz cells, pyramidal tract, cranial nerve nuclei and anterior horn cells. Both UMN and LMN may be involved, but there is no sensory involvement.

Q: What are the types of MND?

A: According to the site of lesion:

1. Spinal cord lesion:
 - Progressive muscular atrophy (PMA): LMN type of lesion.
 - Amyotrophic lateral sclerosis (ALS): Combined UMN and LMN (LMN lesion in upper limbs and UMN lesion in lower limbs).
 - Primary lateral sclerosis (PLS): Pure UMN lesion (rare).
2. Cerebral lesion:
 - Progressive bulbar palsy: Medullary lesion.
 - Pseudobulbar palsy: Cortical lesion.

According to type of lesion:

1. Pure UMN lesion: PLS, pseudobulbar palsy.
2. Pure LMN lesion: PMA, bulbar palsy.
3. Mixed lesion: ALS.

Q: What investigations should be done in MND?

A: No specific test, diagnosis is usually clinical. Investigations are done to exclude other diseases:

- Blood sugar (to exclude diabetic amyotrophy).
- VDRL or *Treponema pallidum* haemagglutination (TPHA) to exclude neurosyphilis.
- Chest X-ray (to exclude bronchial carcinoma).
- X-ray of cervical spine.
- Ultrasonogram of whole abdomen (to see any neoplasm).
- EMG (to confirm fasciculation and denervation).
- Nerve conduction velocity (normal motor and sensory conduction).
- Lumbar puncture and CSF study (no abnormality, only slightly raised protein).
- CT or MRI (brain and spinal cord).

Q: How to treat MND?

A: As follows:

1. No curative treatment.
2. Supportive treatment:
 - Physical rehabilitation.
 - Psychological support.
 - Occupational rehabilitation.
 - Nutritional care: high calorie food supplement, enteral feeding, PEG (percutaneous endoscopic gastrostomy).
 - Speech and communication therapy.
 - Respiratory therapy: Non-invasive positive pressure ventilation (NIPPV, if needed).
 - Home and hospice care, palliative care.

3. Symptomatic treatment:

- Fatigue: Pyridostigmine, amantadine.
- Depression: SSRI, venlafaxine, amantadine.
- Emotional lability: as above.
- Cramps: Quinine sulphate, vitamin E, clonazepam.
- Fasciculation: Carbamazepine.
- Spasticity: Baclofen, tizanidine.
- Sialorrhoea: Hyoscyamine sulphate, scopolamine patch.
- Joint pain: Analgesics (NSAID).
- Insomnia: Zolpidem tartrate.
- Respiratory failure: Bronchodilators.

4. Neuroprotective agents: Riluzole, IGF-1, ASO, vitamin E, Co-enzyme Q-10, neuroprotective factors. Riluzole is a glutamate antagonist that may retard progression and prolong the survival.

Q: What is the **prognosis** of MND?

A: MND is a progressive disorder and its remission is unknown. It is usually fatal within 3 to 5 years. Younger patient with early bulbar syndrome tend to show a more rapid course. Prognosis is relatively better in primary lateral sclerosis and progressive muscular atrophy. Prognosis is worse in:

- Old age.
- Female sex.
- Bulbar onset.

Q: What is the **cause of death**?

A: Bronchopneumonia, respiratory failure resulting from diaphragmatic paralysis and complication of immobility.

Q: What are the **neurological non-metastatic syndromes** of malignancy? (Paraneoplastic syndrome.)

A: As follows:

- Motor neuron disease.
- Sensory neuropathy.
- Mononeuritis multiplex.
- Cranial polyneuropathy.
- Eaton Lambert syndrome.
- Spastic paraparesis.
- Cerebellar syndrome.
- Dementia and encephalopathy.
- Progressive multifocal leucoencephalopathy.

Cause of neurological nonmetastatic syndromes is unknown. It may precede the clinical manifestation of malignancy. Usually, it is common in small cell carcinoma of lung and lymphoma.

FEATURES AND DIAGNOSIS OF INDIVIDUAL MND

Progressive muscular atrophy:

- Weakness, wasting and fasciculation of distal limb muscles, usually starting in small muscles of one or both hands.
- Tendon reflex is lost (due to involvement of anterior horn cell).

Amyotrophic lateral sclerosis:

- LMN lesion in upper limbs: Weakness, wasting, fasciculation and loss of all reflexes **plus**—
- UMN lesion in lower limbs: Spastic paraplegia with exaggerated reflexes and extensor plantar response, or commonly there is generalized hyperreflexia.
- Bulbar and pseudobulbar palsy may follow eventually.

Primary lateral sclerosis:

- Only UMN lesion (both upper and lower limbs).
- Progressive tetraparesis with terminal pseudobulbar palsy may occur.

Progressive bulbar palsy:

- Presents with 3 '**Ds**'—dysarthria, dysphonia and dysphagia. There is nasal regurgitation, dribbling of saliva.
- Speech is nasal, indistinct and slurred.
- Tongue: Wasted, wrinkled and fasciculating.
- There is palatal palsy.
- Gag reflex is absent.
- Site of lesion: Nucleus of lower cranial nerves in medulla (IX, X, XI and XII). Lesion is bilateral and LMN type.
- Common causes:
 - Motor neuron disease.
 - Guillain–Barré syndrome.
 - Syringobulbia.
 - Brainstem infarction.
 - Poliomyelitis.
 - Neurosyphilis.
 - *Neurosarcoid*.

Pseudobulbar palsy:

- Common in women.
- Speech: Nasal, slurred, indistinct and high pitched (so called **Donald Duck** or **hot potato** dysarthria, due to tight immobile tongue).
- Tongue: Small and tight, spastic, unable to protrude, but no wasting or fasciculation.
- Jaw jerk is exaggerated.
- Palatal movement is absent.
- Gag reflex is present.
- The patient is emotionally labile (crying and laughing).
- Site of lesion: Bilateral UMN lesion (supranuclear) involving the pyramidal tract (supranuclear lesion of lower cranial nerves: IX, X, XI, XII).
- Causes:
 - Bilateral repeated cerebrovascular disease (CVD) involving internal capsule (multi-infarct dementia).
 - Demyelinating disease (Multiple sclerosis).
 - Motor neuron disease.

Q: What is the difference between fasciculation and fibrillation of muscle?

A: As follows:

- Fasciculation: Contraction of groups of muscles. It is visible.
- Fibrillation: Contraction of single muscle fibre or unit. It is not visible. Diagnosed by EMG.

Q: What is fasciculation? What are the causes? What is the mechanism?

A: Random spontaneous twitching of a group of muscle fibres or a motor unit that produces movement of the overlying skin or mucous membrane or digits. Fasciculation may be coarse or fine, usually present at rest, but not during voluntary movement. It is usually spontaneous and may be elicited by tapping with finger or hammer over the muscle (this procedure is controversial, as it is not accepted by some neurologists, because it should be spontaneous). If fasciculation is present with weakness and wasting, it indicates LMN lesion.

Mechanism of fasciculation: It is due to spontaneous firing of surviving axons that strive to innervate the muscle fibres that have lost their nerve supply.

Causes of fasciculation:

1. Neurogenic:

- MND.
- Charcot–Marie–Tooth disease.
- Spinal muscular atrophy.
- Radiculopathy (cervical spondylosis, cervical rib).
- Syringomyelia.
- Peripheral neuropathy.
- Creutzfeldt–Jakob disease (CJD).
- Acute stage of poliomyelitis (rarely in old polio).
- Syphilitic amyotrophy.
- Neuralgic amyotrophy.

2. Metabolic:

- Tetany.
- Thyrotoxic myopathy.
- Anticholinergic drugs.
- OPC poisoning.

3. Normal:

- Benign fasciculations (in anxiety or tension. It is usually found around the shoulder joint).
- After exercise in fit adults.
- After tensilon test.
- Muscle cramps.

FRIEDREICH'S ATAXIA

Instruction by the examiner:

- Examine the lower limbs.
- Look at the legs. What are your findings? What else do you want to examine?

Presentation of a Case (the Patient is Usually Young):

- The patient has bilateral pes cavus and cocking of toes.
- There is wasting of muscles of leg.
- Muscle tone and power are diminished in both lower limbs.
- Both knee and ankle jerks are absent.
- Plantar extensor on both sides.
- Sensory test is normal, but loss of vibration and position senses.
- Co-ordination is impaired on both lower limbs (heel–shin test impaired).
- Ataxic gait (cerebellar).
- Rombergism is positive.
- Other findings: The patient may have hearing or visual aid (mention, if any). Also, kyphoscoliosis.

My diagnosis is **Friedreich's ataxia**.

Q: What else do you want to see?

A: As follows:

- Palate (high arched).
- Spine (kyphoscoliosis).
- Signs of cerebellar lesion (see in cerebellar lesion).
- Eyes (nystagmus in 25%, fundoscopy shows optic atrophy in 30%, retinal atrophy and retinitis pigmentosa).
- Heart: cardiomyopathy (hypertrophic cardiomyopathy, may cause sudden death), ECG change in 50% cases.
- Sensory neural deafness (in 10% cases).

Q: What are the causes of high arched palate?

A: As follows:

- Friedreich's ataxia.
- Marfan's syndrome.
- Homocystinuria.
- Turner's syndrome.
- Tuberous sclerosis.

Q: Why absent tendon reflex, but extensor plantar response?

A: Because of combination of pyramidal lesion, dorsal column and dorsal root lesion. Also, there is involvement of peripheral sensory fibres that leads to sensory disturbance in the limbs and depressed tendon reflex.

Q: What are the causes of pes cavus?

A: See in 'Charcot–Marie–Tooth disease'.

Q: What are the **differential diagnoses** of Friedreich ataxia?

A: As follows:

- Multiple sclerosis.
- Tabes dorsalis.
- Spinocerebellar degeneration.



Unilateral Pes cavus



Bilateral Pes cavus

READ THE FOLLOWING TOPICS IN RELATION TO FRIEDRICH'S ATAXIA

Q: What is **Friedreich's ataxia**? What is the **cause**? What are the **features**?

A: It is the common type of hereditary ataxia inherited as autosomal recessive trait and in some cases, inherited as autosomal dominant.

Cause: Unknown. Mutation of *FRDA* gene in chromosome 9. The mutation is abnormal expansion of trinucleotide repeat within a gene that codes for protein 'Frataxin', whose function is to prevent intra-mitochondrial iron overloading.

Features of Friedreich's ataxia are:

1. Family history: May be present.
2. Usual onset: Young, <15 years (8 to 16 years).
3. Presentations: Progressive difficulty in walking (due to ataxia of lower limbs), truncal ataxia, weakness of lower limbs and dysarthria.
4. Signs are:
 - Cerebellar signs (dysarthria, nystagmus, intention tremor, ataxic gait).
 - Posterior column: Absent vibration and position sense, positive Rombergism.
 - Corticospinal tract sign: Plantar extensor, weakness.
 - Peripheral nerve: Absent reflexes in lower limbs, wasting of muscles.
5. Diabetes mellitus (10%).
6. Associated with kyphoscoliosis, pes cavus, cocking of toes, optic atrophy (25%), spina bifida and hypertrophic cardiomyopathy (50%, may cause sudden death), hearing loss (10%).
7. Normal mentation (may have mild dementia).
8. Prognosis: Usually progresses slowly, death occurs before 40 years of age (usually 20 years after the onset of symptoms due to cardiac and respiratory complications).
9. Becomes chair bound 9 to 15 years after onset of symptoms. May be static and survive up to 60 years.

*N.B.: In young patient with pes cavus **plus** combination of cerebellar lesion (bilateral), UMN lesion (extensor plantar) and posterior column lesion (loss of vibration and position senses) is highly suggestive of Friedreich's ataxia.*

Q: What are the **sites** of lesion in Friedreich's ataxia?

A: As follows (there is progressive degeneration):

- Cerebellum.
- Spinocerebellar tract.
- Posterior column.
- Dorsal root ganglia.
- Degeneration of peripheral sensory fibres.
- Corticospinal tract (lateral column).
- Eye (primary optic atrophy).

Q: What are the different **types** of hereditary ataxias?

A: It may be of different types, with different patterns of inheritance:

1. Autosomal recessive:
 - Friedreich's ataxia.
 - Ataxia telangiectasia.
 - Ataxia with vitamin E deficiency.
 - Abetalipoproteinaemia.
2. Autosomal dominant:
 - Spinocerebellar ataxia type 1 to 28.
 - Episodic ataxia.
 - DRPLA (Dentato-rubro-pallidoluysian atrophy).
3. X-linked:
 - Fragile X tremor ataxia syndrome (FXTAS).
 - Adrenoleukodystrophy.
4. Mitochondrial:
 - Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS).
 - Myoclonic epilepsy with ragged-red fibres (MERRF).
 - Kearns–Sayre syndrome (KSS).

Q: What are the causes of **combined** cerebellar, pyramidal and dorsal column signs?

A: As follows:

- Multiple sclerosis.
- Friedreich's ataxia.
- Spinocerebellar degeneration.
- Syphilitic meningomyelitis.
- Arnold–Chiari malformation.

Q: What **investigations** should be done in Friedreich's ataxia?

A: As follows:

- CBC, ESR.
- Blood sugar (high in 10%).
- Urine RME (sugar may be present).
- Chest X-ray (cardiomegaly).
- ECG (arrhythmia).
- MRI of brain and spinal cord (shows atrophy of cerebellum and spinal cord).
- NCS (shows conduction velocity in motor fibres is normal or mildly reduced, but sensory action potentials are small or absent).

Q: How to **manage** this patient?

A: There is no specific therapy. However, the following measures should be taken:

- Physiotherapy and exercise.
- Orthopaedic surgery to correct scoliosis, pes cavus and other deformities.
- Ankle or foot orthoses.
- Walking aids.
- Occupational therapy.
- Visual aids.
- Hearing aids.
- Treatment of related conditions like diabetes mellitus, hypertrophic cardiomyopathy, arrhythmia.

CEREBELLAR LESION

Instruction by the examiner:

- Examine for cerebellar signs.
- Talk with the patient. What is your finding? (Scanning speech). What else do you want to examine? (I want to examine to see the cerebellar signs.)

To examine for cerebellar signs, proceed as follows:

- Look carefully: Head nodding (called **titubation** either **to** and **fro** movement—like ‘**yes–yes**’ or rotatory movement like ‘**no–no**’).
- Shoulder is tilted towards the site of lesion (lower down).
- Talk with the patient: Scanning or staccato speech (with bilateral lesion).
- Eye: Nystagmus (jerky, horizontal and coarse with increase in amplitude on looking towards the site of lesion). Skew deviation of the eyes: Ipsilateral down and inwards, contralateral up and out.
- Finger–nose test: Positive (look for past point and intention tremor that increases on approaching the target).
- Dysdiadochokinesis (rapid alternating pronation and supination of forearm), tap one hand with its palmar and dorsal aspect on the other hand alternately.
- Rebound phenomenon: Ask the patient to hold both the arms out and front and keep it. Push both arms and release suddenly. Ipsilateral arm will fly past the starting point (it is due to failure of reflex arrest).
- Also ask the patient to extend the arms and look for arm drift due to hypotonia of agonist muscles.

Now, examine the **lower limbs** for cerebellar signs:

- Heel–shin test (inco-ordination).
- Ipsilateral hypotonia (it is due to loss of facilitatory influence on spinal motor neuron) and diminished muscle power.
- Knee jerk (pendular).
- Dysdiadochokinesis of foot (ask the patient to tap your hand by his/her foot).
- Gait (reeling or drunken): Patient will stagger towards the affected side during walking.

Presentation of a Case:

- There is titubation (mention, if any) and tilting of shoulder towards the right or left side.
- Speech is scanning or staccato (jerky, slurred and explosive, the patient talks syllable by syllable).
- There is horizontal and coarse nystagmus.
- Finger–nose test is positive (right, left or both) and intention tremor is present, which is worse as the finger approaches the target.
- Dysdiadochokinesis: Present.
- Heel–shin test: Impaired (inco-ordination).
- There is hypotonia in the right (or left) lower limb.
- Knee jerk is pendular (mention, if any).
- Gait: Reeling or drunken.

My diagnosis is **Cerebellar lesion (mention the side, right or left).**

Q: What do you think are the **causes** in this case?

A: Mention the causes according to the age of the patient:

If the patient is young, the causes are:

- Friedreich's ataxia.
- Multiple sclerosis.
- Wilson's disease.
- Drugs (phenytoin, carbamazepine).
- Others: Hypothyroidism, trauma.

If the patient is middle-aged or elderly, causes are:

1. Multiple sclerosis.
2. Brainstem vascular lesion.
3. Paraneoplastic syndrome.
4. Alcohol and drugs.
5. Secondary deposit in cerebellum.
6. Degenerative lesions: Progressive cerebellar degeneration, Olivo-ponto-cerebellar degeneration, Shy-Drager syndrome (Multiple system atrophy), Creutzfeldt-Jakob's disease.

Q: What are the **drugs** causing cerebellar syndrome?

A: Phenytoin, carbamazepine, lithium, phenobarbitone, sometimes chemotherapy agents.

Q: Mention **one investigation** to confirm cerebellar lesion.

A: MRI of brain.

Q: What is the nature of the **cerebellar tremor**?

A: Intension tremor, which is absent at rest but appears during voluntary activity, especially when approaching to a target.

Q: What are the **findings** in **vermis lesion**?

A: As follows:

- Ataxia is usually truncal, causes difficulty in standing and sitting unsupported with broad based gait.
- Only lower limbs are affected. When limbs are tested separately on bed, usually little or no sign.
- Romberg's sign may be positive (same on closing and opening of the eye—to differentiate from sensory ataxia).

Q: What is the **cause** of vermis lesion?

A: Alcohol, which causes atrophy of anterior part of vermis (sparing the upper limb).

Q: When to suspect only **midline lesion**? What are the **causes**?

A: When only truncal ataxia is present, there is abnormal speech and heel-toe walking is positive. Causes are:

- Paraneoplastic syndrome.
- Midline space occupying lesion.

Q: What are the **findings** in cerebellar hemisphere **lesion**?

A: Ipsilateral limb ataxia.

READ THE FOLLOWING TOPICS IN RELATION TO CEREBELLAR LESION

Causes of cerebellar lesion:

1. Vascular (cerebellar haemorrhage or infarction, arteriovenous malformation, brainstem vascular lesion).
2. Demyelinating (Multiple sclerosis).
3. Drugs (phenytoin, carbamazepine).
4. Alcohol.
5. Toxins (carbon monoxide poisoning, solvent abuse and lead poisoning).
6. Neoplasm (haemangioblastoma, medulloblastoma, astrocytoma, secondary deposit, compression by acoustic neuroma).
7. Infection (cerebellar abscess from otitis media, HIV and Kuru disease).
8. Inherited (Friedreich's ataxia and other hereditary ataxias).
9. Cerebellar syndrome of malignancy (paraneoplastic syndrome).
10. Cerebellar syndrome:
 - Shy–Drager syndrome (Multiple system atrophy).
 - Steele–Richardson–Olszewski syndrome.
 - Creutzfeldt–Jakob disease.
 - Wilson's disease.
11. Others:
 - Hypothyroidism.
 - Arnold–Chiari lesion.
 - Trauma (punch-drunk syndrome).
 - Cerebral palsy.
 - Hydrocephalus.

Q: What are the **functions** of cerebellum?

A: It is concerned with the control of voluntary movements, maintenance of posture and balance.

Q: What are the malignancies causing **paraneoplastic syndrome of cerebellum**?

A: Carcinoma of ovary, uterus, breast, small-cell carcinoma of lung, Hodgkin's lymphoma etc. This is probably immune mediated. Cerebellar lesions are usually bilateral (unilateral lesion is against paraneoplastic cerebellar lesion). Two antibodies are recognized for different malignancies:

- Anti-Yo (anti-Purkinje cell antibody): Related to carcinoma of ovary, uterus and breast.
- Anti-Hu (anti-neuronal cancer antibody): Related to small cell carcinoma of lung, carcinoma of prostate, sarcoma, neuroblastoma.

N.B.: Remember that signs of cerebellar lesion occur on the same side of lesion, because most cerebellar fibres cross twice in brainstem while entering and exiting the cerebellum.

Q: What are the **primary tumours** of cerebellum?

A: Medulloblastoma and astrocytoma.

Q: How the cerebellar signs are localized?

A: As follows:

- **Gait ataxia:** inability to do tandem walking (heel to toe walking)—lesion in anterior lobe (palaeocerebellum).
- **Truncal ataxia:** drunken gait, titubation—lesion in flocculonodular or posterior lobe (archicerebellum).
- **Limb ataxia:** especially upper limb and hypotonia—lesion in lateral lobe (neocerebellum).

Q: What are the signs of cerebellar lesion?

A: As follows:

- Titubation.
- Tilting towards the site of lesion.
- Nystagmus (horizontal).
- Scanning speech.
- Intention tremor.
- Incoordination.
- Dysdiadochokinesis.
- Past-pointing (dysmetria).
- Ataxia.
- Hypotonia.
- Diminished tendon reflex (knee jerk may be pendular).

PARKINSON'S DISEASE

Instruction by the examiner:

- Look at the face. What are your findings? What else do you want to examine?
- Look at the hands (resting tremor). What else do you want to examine?

In a patient with Parkinson's disease, proceed to examine as follows:

1. In the face: Look at the following points—
 - Titubation of head.
 - Mask like, expressionless face, less blinking with staring looks (frequency of spontaneous blinking is reduced, called serpentine stare). Blepharoclonus may be present (tremor of eyelids, when eyes are gently closed).
 - Dribbling of saliva.
2. Talk to the patient:
 - Speech—slow initiation, husky, slurred, indistinct, lacking intonation, low volume and monotonous (or mutism).
 - Palilalia is present (repetition of the end of a word).
3. Glabellar tap (Myerson's sign): Positive (tap the forehead above the bridge of nose repeatedly). In normal person, blinking will stop after 3 to 5 blinks, but in parkinsonism, the patient continues to blink. This sign is unreliable.
4. Look at the tremor (see below): Present at rest, tremor disappears or reduces with activity or holding something.
5. Rigidity: Lead pipe (better seen in elbow) or cogwheel (better seen in wrist).
6. Tests for hypokinesia:
 - Ask the patient to do fastening of button (patient is unable or can do slowly).
 - Ask to write (micrographia, handwriting is tremulous and untidy).
 - Ask to touch tip of all fingers with thumb successively or ask to count such as one, two . . . (there is slow initiation, patient is unable or can do slowly or progressive reduction of amplitude of each movement during counting).
 - Ask the patient to do rapid fine finger movement (like piano playing): It becomes indistinct, slurred and tremulous.
 - Ask the patient to open and close hands repeatedly or ask to tap with foot or hand (it gradually becomes slow and smaller in amplitude).
 - Ask the patient to perform 2 different simultaneous motor acts (patient is unable to do so).
7. Ask the patient to stand and see the position (there is flexed and stooped attitude).
8. Gait: Ask to walk and to turn quickly (there is difficulty in starting to walk, called **freezing**, paucity of movement, less swinging of arms and flexed attitude, inability to turn rapidly, called **fractionated** turn).

Presentation of Case No. 1 (by Looking at the Face):

- The patient has titubation of head (mention, if any).
- Face is mask-like, expressionless with less blinks of the eyes, staring look and dribbling of saliva.

My diagnosis is **Parkinson's disease**.

Q: What else do you like to examine?

A: Comment on **resting tremor**, if present. Then tell, 'I would like to examine...':

- Speech (talk to the patient).
- Glabellar tap (positive).
- Muscle tone (rigidity).
- Hypokinesia (see above).
- Gait (see below).

Presentation of Case No. 2: By Looking at Tremor (After Describing Tremor, Describe Face as in Case No. 1 Plus Relevantants)—

- There is resting tremor with pill rolling movement of right (or left) thumb, which disappears after voluntary movement or holding something.
- Rigidity is present (which is cog wheel or lead pipe).
- There is hypokinesia.
- Speech (as above).
- Gait (ask the patient to raise from chair, walk, turn quickly, stop and start):
 - Difficulty in starting to walk. Once started, there is rapid, small, shuffling steps (hardly raising the foot from ground), as if trying to keep up with his own centre of gravity.
 - During walking: Stooped or flexed attitude with less swinging of arms, also—
 - Rapid walking and difficulty in stopping himself with tendency to run (festination).
 - He has difficulty in rapid turning (fractionated gait).

My diagnosis is **Parkinson's disease**.

Q: What do you think the **causes** of Parkinsonism in this case?

A: Mention the causes according to the age:

In elderly patients, the causes are:

- Idiopathic or paralytic agitans (common cause). Mention other causes (as below), if asked:
- Drugs.
- Post-encephalitic Parkinsonism.
- Neurosyphilis.
- Trauma (to head).
- Cerebral tumour.

In young patients, the causes are:

- Post-encephalitic Parkinsonism.
- Drugs.
- Wilson's disease.
- Trauma (to head).



Face in a case of Parkinsonism



Parkinsonism (flexed attitude)



Myerson's sign

Q: What **history** do you like to take?

A: As follows:

- History of head injury (e.g., punch drunk syndrome).
- Drugs (phenothiazine, butyrophenone, metoclopramide, tetrabenazine, α -methyl dopa, lithium, valproic acid).
- History of fever, convulsion, headache, coma (post-encephalitic).
- Jaundice, chronic liver disease (Wilson's disease).
- History of headache, vomiting, convulsion (cerebral tumour).

Q: Describe the **tremor** in Parkinsonism.

A: As follows:

- Involuntary, unilateral, coarse, resting tremor in hand.
- Initially, there is pill rolling movement of thumb and index finger, flexion-extension of fingers, abduction-adduction of thumb, pronation-supination of forearm.
- Later, tremor may affect arms, legs, feet, jaw and tongue.
- It disappears or reduces during voluntary activity and sleep, increases with emotion or anxiety.
- Tremor is absent in 1/3rd cases at presentation, also may be absent throughout its course in some cases.

Q: What are the types of **rigidity** in Parkinsonism?

A: 2 types:

- Lead pipe: Resistance is uniform throughout the passive movement (better seen in elbow and knee).
- Cog wheel: rigidity is interrupted by tremor (better seen in wrist joint). It is due to exaggerated stretch reflex interrupted by tremor. It is more common in Parkinsonism.

N.B.: Sometimes, rigidity of the examining limb is increased with simultaneous active movement of the opposite limb (it is one type of reinforcement).

Q: What are the features of **hysterical rigidity**?

A: In hysterical rigidity, muscle tone increases more and more with increasing manoeuvre of the affected limb. The more the limbs are moved or examined, the more rigid it gets.

Q: What is dyskinesia or akinesia? Describe dyskinesia or hypokinesia in Parkinsonism.

A: Dyskinesia is the difficulty in initiating motor activity or poverty or slowing of movement (called bradykinesia).

In Parkinsonism, there is delay or slowness in initiating or slowness of movement (bradykinesia). Also, progressive slowing, smaller in amplitude and speed of repetitive movements, such as opening and closing the hand or finger tapping. There is difficulty in executing two motor acts simultaneously.

Q: What are the differences between essential tremor and Parkinsonian tremor?

A: As follows:

Features	Essential Tremor	Parkinsonian Tremor
1. Stimulus	Tremor is present with voluntary movement, rarely at rest (called action tremor)	Tremor is present at rest
2. Family H/O tremor	Yes	No
3. Body parts involved	Hands, head	Hands, legs, rarely head
4. Distribution at onset	Bilateral and symmetrical	Unilateral and asymmetrical
5. Sensitivity to alcohol	Yes	No
6. Course	Stable and slowly progressive	Progressive

Q: Describe the typical gait in Parkinsonism.

A: It is characterized by:

- Rapid small shuffling step (festination) with stooping forward and narrow base in order to avoid falling, hardly raises the foot from the ground and feet may scrap the ground.
- The patient seems to catch up with his own centre of gravity.
- There is less swinging of the arms during walking and has difficulty in stopping himself.
- He has difficulty in rapid turning (fractionated gait) and turns en block.
- Obstacles cause the patient to freeze in place.

Q: What are the other abnormal gaits in Parkinsonism?

A: As follows (these tests should not be done at the bedside):

- Propulsion: If the patient is pushed from behind, he is unable to stop himself and may fall forward.
- Retropulsion: If the patient is pushed from front, he is unable to stop himself and may fall backward.
- Kinesia paradoxa: The patient is unable to initiate a movement but once started, can complete the whole act (may run down the stairs, but cannot stop at the bottom) or the patient is unable to initiate a movement, but during emotion or fear (e.g., fire in the house), can perform the movement (even run out from the house).
- Synkinesia: Voluntary movement of one part is associated with involuntary movement of opposite part of the body (found in upper limb e.g., voluntary closing-opening of right hand causes involuntary closing-opening of left hand).

Q: What are the reflexes and plantar response in Parkinsonism?

A: All the reflexes and plantar responses are normal. It may be difficult to elicit because of rigidity. Plantar is flexor. It may be extensor if associated with the following disorders:

1. Post-encephalitic Parkinsonism.
2. Other diseases (called atypical Parkinsonian syndrome):
 - Shy–Drager syndrome (Multiple system atrophy).
 - Steele–Richardson–Olszewski syndrome (progressive supranuclear palsy).
 - Olivopontocerebellar atrophy (OPCA).
 - Cortico-basal degeneration (CBD).

READ THE FOLLOWING TOPICS IN RELATION TO PARKINSONISM

Q: What is Parkinsonism?

A: It is a syndrome consisting of tremor, rigidity, bradykinesia and loss of postural reflexes.

Q: What is Parkinson's disease?

A: Parkinson's disease (paralysis agitans) is the primary or idiopathic Parkinsonism. It is a neurodegenerative disorder due to involvement of basal ganglia, characterized by slowness of movement, rigidity, tremor and loss of postural reflex.

Q: What is Parkinsonian plus syndrome?

A: It is characterized by features of Parkinsonism associated with other degenerative disease of cerebellum and pyramidal system, such as progressive supranuclear palsy (Steele–Richardson–Olszewski syndrome), olivopontocerebellar degeneration, nigrostriatal degeneration, primary autonomic failure (Shy–Drager syndrome, also known as multiple system atrophy). Features are:

- Poor response to levodopa.
- Symmetrical features, especially at an early stage.
- Early onset of postural instability, fall, dementia, hallucinations, autonomic dysfunction etc.
- Presence of pyramidal signs (not due to previous stroke or other pathology), cerebellar signs or ocular signs (e.g., nystagmus, gaze palsy).
- Truncal symptoms more prominent than appendicular symptoms.
- Absence of structural aetiology such as a normal pressure hydrocephalus (NPH).

Q: What are the diagnostic criteria for Parkinsonism?

A: **Triad** of (Remember the formula **TRH**. According to Brain Bank criteria, postural instability is another criterion).

- Tremor at rest (4 to 6 Hz).
- Rigidity.
- Hypokinesia.

Q: What is the pathological change in Parkinsonism?

A: In idiopathic Parkinsonism, there is progressive degeneration of pigmented dopaminergic neurons of substantia nigra and formation of eosinophilic cytoplasmic inclusions in neurons (Lewy bodies, which contain α synuclein and ubiquitin). Lewy body is the pathological hallmark of Parkinson's disease. Hence, there is deficiency of dopamine (and melanin) with relative increase in cholinergic transmission (imbalance between dopamine and acetylcholine).

Q: What is the mental status in Parkinsonism?**A:** As follows:

- Initially, intellect and memory are normal. There may be slowness of thought and memory retrieval (bradyphrenia) and subtle personality changes.
- Depression occurs in 1/3rd patients.
- Global dementia (20%) and psychosis.
- Drug treatment may precipitate acute confusion.

Q: What are the stages of Parkinsonism?**A:** As follows:

- Stage I: Unilateral involvement (hemiplegic Parkinsonism).
- Stage II: Bilateral involvement but no postural abnormality.
- Stage III: Bilateral involvement with mild postural abnormality.
- Stage IV: Stage 3 plus severe postural abnormality requiring substantial help.
- Stage V: Severe disease. The patient is restricted to bed and wheel chair.

Q: What are the causes of Parkinsonism?**A:** Unknown, multiple factors are responsible:

1. Paralysis agitans (Idiopathic Parkinson's disease, common, 80% case). Usually occurs in middle aged or elderly.
2. Post-encephalitic (encephalitis lethargica and Japanese B encephalitis).
3. Drugs: Phenothiazines (chlorpromazine, prochlorperazine), butyrophenones (haloperidol), metoclopramide, tetraabenazine, methyl dopa, sodium valproate, lithium.
4. Neurosyphilis.
5. Poisoning: Carbon monoxide, manganese and MPTP (methyl-phenyl-tetrahydropyridine) may occur in drug addicts.
6. Herbicide (paraquat, may be related to MPTP).
7. Trauma (punch-drunk syndrome and repeated head injury).
8. Genetic (Wilson's disease and Huntington's disease).
9. Cerebral tumour (involving basal ganglia).
10. Parkinsonian plus (when associated with features or pathology of other disease):
 - Shy-Drager syndrome (Multiple system atrophy).
 - Steele-Richardson-Olszewski syndrome (progressive supranuclear palsy, characterized by inability of movement of eye vertically or laterally and dementia).
 - Olivo-ponto-cerebellar degeneration.
11. Creutzfeldt-Jakob disease.
12. Hypoparathyroidism.
13. Normal pressure hydrocephalus (triad of urinary incontinence, gait apraxia and dementia).
14. Atherosclerotic Parkinsonism (characterized by stepwise progressive broad based gait and pyramidal signs).

Q: What investigations should be done in Parkinsonism?

A: Diagnosis is usually clinical. Investigations are done for specific cases or to exclude other diseases:

1. CT scan or MRI (may be done if there is pyramidal, cerebellar and autonomic involvement or doubtful diagnosis).
2. In patient <50 years, screening for Wilson's disease:
 - Serum ceruloplasmin (low).
 - Serum copper (high serum free copper).
 - 24 hour urinary copper (high). Following penicillamine therapy, 24 hour urinary copper >25 mmol is confirmatory.
 - Liver function tests may be done.
 - Liver biopsy with quantitative measurement of copper (less done).
3. Functional dopaminergic imaging (SPECT or PET) is abnormal, even at early stages. But does not differentiate between different forms of degenerative parkinsonism and so, it is not specific for PD.

Q: How to differentiate between post-encephalitic Parkinsonism and paralytic agitans?

A: As follows:

Criteria	Post-Encephalitic	Paralytic Agitans
1. Age	Any, commonly young	Elderly or middle age
2. Onset	Sudden	Insidious
3. Previous history	Encephalitis, fever and headache	No particular history
4. Complaints	Mainly rigidity, also impaired higher functions, excess salivation (autonomic features), little or no tremor	Mainly tremor
5. Symmetry	Fairly symmetrical rigidity and hypokinesia	Asymmetrical
6. Eye signs: • Oculogyric crisis • Ophthalmoplegia • Pupil	Present Present Abnormal (dilated, irregular)	Absent Absent No abnormality
7. Neurological features: • Dystonia, dementia, chorea, hemiparesis • Rigidity • Tendon reflexes • Plantar response	• Present • Usually lead pipe (due to absence of tremor) • Brisk • Extensor	• Absent • Usually cogwheel • Normal • Flexor
8. Levodopa	Less sensitive	Sensitive
9. Prognosis	Not good	Slowly progressive
10. Lewy body	Absent	Present

Q: What is oculogyric crisis?

A: It is an involuntary, sustained upward and outward deviation of the eyes. Causes are:

- Post-encephalitic Parkinsonism.
- Drugs (commonly phenothiazines).
- Petit mal epilepsy.

Q: What are the treatment modalities in Parkinsonism?**A:** As follows:

- Treatment of cause and withdrawal of offending drugs, if any.
- Symptomatic treatment of tremor, rigidity and bradykinesia.
- Physiotherapy and speech therapy.
- Surgical treatment.
- Occupational therapy and rehabilitation.

Q: How to treat Parkinson's disease?**A:** Drug is usually not given in mild case because of side effects. Should be started if significant disability and symptoms.

1. Combination of levodopa and dopa-decarboxylase inhibitor is the treatment of choice. Available combinations are levodopa and carbidopa (110 or 275 mg), levodopa and benserazide (62.5 mg). Drugs should be started with lowest possible dose and gradually increased as needed.
2. Tremor may be controlled by anticholinergic drugs (such as trihexyphenidyl, benztropine, orphenadrine, benzhexol, biperiden). Less used because of side effects (dry mouth, blurred vision, constipation, urinary retention).
3. Other drugs: Amantadine, MAO-B inhibitor (selegiline, rasagiline), catechol-o-methyl transferase (COMT) inhibitors (entacapone, tolcapone), dopamine agonist (pergolide, bromocriptine, lisuride, ropinirole, pramipexole, apomorphine) may be used.
4. General measures:
 - Physiotherapy and speech therapy.
 - Occupational therapy and rehabilitation.
5. Other measures:
 - Cognitive impairment and psychiatric symptoms may be helped by rivastigmine.
 - Trazodone is helpful in treating depression and insomnia.
 - For psychosis, confusion or hallucination: Atypical antipsychotic can be given.

*N.B.: Levodopa is absolutely contraindicated in presence of melanoma.***Q: What is the role of surgery in Parkinsonism?****A:** Surgery may be considered in some cases, if failure of medical therapy. Options are:

- Stereotactic thalamotomy (ventrolateral nucleus of thalamus): Usually unilateral, bilateral thalamotomy is not recommended. It relieves tremor on the contralateral side (but little effect on bradykinesia, rigidity, motor fluctuation and dyskinesia).
- Pallidotomy: Destruction of a part of globus pallidus interna is done. It helps in improvement of contralateral features like tremor, bradykinesia and rigidity. Also reduces dyskinesia. Bilateral pallidotomy is not recommended.
- Subthalamotomy: Involves destruction of a part of subthalamic nucleus. It improves contralateral features like tremor, bradykinesia and rigidity.
- Deep brain stimulation: It is a procedure that has replaced the surgery. A lead is implanted into the targeted brain structure such as thalamus, globus pallidus interna or subthalamic nucleus. Then it is connected to an implantable pulse generator, usually in subclavicular area, that delivers high frequency electrical discharge. It can be used to stimulate bilateral lesion.
- Foetal midbrain or adrenal tissue implantation in basal ganglia. This is helpful in younger patient. Cannot be used regularly because of ethical issues.

Q: What are end of dose deterioration and on-off phenomenon?

A: After 3 to 5 years of levodopa therapy, there may be fluctuating response to levodopa in 50% patients. These include:

- **End of dose dyskinesia** (wearing-off effect): Due to progression of disease and loss of capacity to store dopamine, duration of action of levodopa becomes progressively shorter. As a result, the patient complains of freezing and rigidity before the next dose of levodopa. This may be managed by dividing levodopa into smaller and frequent doses. Also by using slow release preparations or adding dopamine agonist or adding amantadine.
- **On-off phenomenon:** After prolonged use, drug may become less effective. There is sudden, unpredictable change in response in which periods of severe Parkinsonism (freezing and immobility—**off** period) alternate with periods of dopamine-induced dyskinesias, agitation, chorea, dystonic movements (**on** period). This can be managed by lowering the dose of levodopa or adding selegiline with levodopa. COMT inhibitor or dopamine agonist may be added.

Q: What is the role of protein in treatment of PD?

A: Amino acids in dietary protein compete with levodopa for intestinal absorption and transport across blood brain barrier. So, efficacy of levodopa is less with high protein diet.

Q: What are the extrapyramidal effects of phenothiazine group of drugs (or antipsychotic drugs)?

A: As follows:

- Parkinsonism (tremor is less and responds to anticholinergic drugs than L-dopa).
- Dystonia (by prochlorperazine and metoclopramide).
- Akathisia (it is the uncontrolled restlessness with repetitive and irresistible need to move).
- Tardive dyskinesia: Characterized by orofacial dyskinesia including lip smacking, chewing, pouting and grimacing. It is usually due to use of phenothiazines and butyrophenones for at least 6 months. May be worse or may persist after the withdrawal of drug. Tetrabenazine may help.
- Chorea.

CHOREA

Instruction by the examiner:

- Look at the patient. What is your diagnosis? What else do you want to see or what relevants do you like to see?

Presentation of a Case (by Looking):

- There is an involuntary, non-repetitive, quasi-purposive, irregular, jerky movement of the arm, head and also the whole body, which is present at rest and increases after activity.
- The movements are randomly distributed and moves from one part of the body to other.
- The patient looks clumsy and restless (may keep dropping object).
- There may be writhing or dancing movement of the limbs (mention, if any).

My diagnosis is **Chorea (or Choreo-athetosis)**.

Q: What else do you want to examine?

A: I want to examine:

- Muscle tone (there is **hypotonia**).
- Ask the patient to protrude the tongue: the patient is unable to keep the tongue protruded out (It darts in and out, called serpentine movement or **jack in the box**).
- Ask the patient to raise both arms above the head opposing the palmar side (Patient's hands will **sway outward**, there will be pronation of forearm).
- Perform handshake with the patient (There is alternate squeezing and gripping of patient's finger or lack of sustained hand gripping called, **milkmaid's grip**).
- Ask the patient to raise both his/her arms in front (There may be flexion of wrist joint and hyperextension of metacarpophalangeal and finger joints, called **dinner fork deformity or choreic hand**).



Chorea



Chorea



Chorea

Q: What history should be taken?**A:** I shall take:

- Family history (in Huntington's chorea and Wilson's disease).
- Drugs (neuroleptics, phenothiazine, tricyclic antidepressant, oral contraceptive pill, phenytoin, L-dopa).
- In females: Oral contraceptive pill and pregnancy.
- History of encephalitis.
- In young patients or children: History of sore throat or rheumatic fever (rheumatic chorea).
- Others: History of thyrotoxicosis, polycythaemia rubra vera (PRV) and SLE.

READ THE FOLLOWING TOPICS IN RELATION TO CHOREA
Q: What is chorea?

A: It is the involuntary, non-repetitive, quasi-purposive, irregular and jerky movements of one or more parts of the body due to extrapyramidal lesion. Chorea may be unilateral or generalized, sometimes the patient attempts to disguise this by completing the involuntary movements with a voluntary movement. It worsens with anxiety or activity and disappears during sleep (chorea means dance, from a Greek word).

Q: What is the site of lesion in chorea?

A: Caudate nucleus of basal ganglia. Also, it is due to the excess activity in corpus striatum with dopaminergic drugs, which are used to treat Parkinsonism. Dopaminergic pathways dominate over cholinergic transmission.

Q: What are the causes of chorea?**A:** As follows:

1. Rheumatic chorea (post-streptococcal called Sydenham's chorea or St. Vitus dance).
2. Senile chorea.
3. Hereditary (Huntington's chorea, Wilson's disease, benign familial chorea, paroxysmal choreo-athetosis, spinocerebellar ataxia and neuro-acanthocytosis).
4. Drug induced (see above).
5. Pregnancy (called chorea gravidarum).
6. Encephalitis lethargica.
7. Following stroke.
8. Others (rare):
 - Polycythaemia rubra vera and other myeloproliferative disorders.
 - SLE and antiphospholipid syndrome.
 - Endocrine (thyrotoxicosis, idiopathic hypoparathyroidism and hypoglycaemia).
 - Kernicterus.
 - Cerebral birth injury.
 - Cerebral trauma.
 - Creutzfeldt-Jakob disease.
 - Henoch-Schönlein purpura.
 - Vascular (lacunar infarction and arteriovenous malformation).
 - Carbon monoxide poisoning.

Q: How to treat chorea?**A:** As follows:

- Reassurance and treatment of primary cause (if any).
- Drugs that may be helpful are phenothiazine, butyrophenones (haloperidol), tetrabenazine and sodium valproate.

Q: What is Sydenham's chorea? How to treat?**A:** It occurs in rheumatic fever due to the involvement of CNS that develops after streptococcal infection and there is diffuse mild encephalitis. History of rheumatic fever may be present in one third cases.

- Common in children and adolescents, more in female, age 5 to 15 years.
- Chorea is associated with emotional instability, irritability, inattentiveness, confusion and fidgety. Speech is often affected.
- It manifests for long time, may be 6 months after the initial infection.
- Other features of rheumatic fever may be absent, when chorea is present.
- Carditis may be the first manifestation and rheumatic heart disease may occur.
- Fever is unusual and ESR, ASO titre and CRP are usually normal.
- It is usually self limiting and recovers within weeks or 1 month (may be 5 to 15 weeks). Recurrence may occur in 20% cases. Occasionally, it may relapse during pregnancy (called chorea gravidarum) or in those who use oral contraceptive pills.

Treatment:

- No treatment is necessary in most cases as recovery is spontaneous.
- In severe chorea: Benzodiazepine, haloperidol, tetrabenazine or valproate may be given.
- Penicillin prophylaxis as in rheumatic fever.

Q: Name some involuntary movements.**A:** As follows:

- Tremor.
- Chorea.
- Athetosis.
- Hemiballismus.
- Myoclonus.
- Tic.
- Torsion dystonia (it may be generalized or localized such as spasmodic torticollis, writer's cramp, oromandibular dyskinesia, blepharospasm and hemiplegic dystonia).

Q: What is Huntington's chorea?**A:** It is a disorder, inherited as autosomal dominant, in which chorea is associated with progressive dementia. Gene responsible is on the short arm of chromosome 4. Usually present in adult, during third to fourth decade. Chorea involves the lower limb more than upper limb. Occasionally, there is juvenile onset where Parkinsonism is the main feature.Huntington's chorea is **diagnosed** by:

- Family history.
- Chorea followed by progressive dementia (also producing a dancing sort of gait).

Q: What are the other features of Huntington's disease?

A: Other features of Huntington's disease, chorea may be associated with the following:

- Bradykinesia.
- Myoclonus.
- Dystonia, dysarthria, dysphasia.
- Ataxia.
- Slow, saccadic eye movements.
- Cognitive impairment.
- Psychiatric disturbance.
- Rigidity.

Q: What are the pathological changes in Huntington's chorea?

A: Cerebral atrophy with neuronal loss in caudate nucleus and putamen.

Q: What are the changes of neurotransmitters in Huntington's chorea?

- Reduction of acetylcholine transferase and glutamic acid decarboxylase (GAD) in the corpus striatum.
- Depletion of α -aminobutyric acid (GABA), substance P, angiotensin-converting enzyme and met-enkephalin in substantia nigra.
- High somatostatin level in corpus striatum.

Q: How to investigate?

A: As follows:

- MRI of brain: shows atrophy of caudate nucleus and also cerebral atrophy.
- DNA analysis.

Q: How to treat?

A: There is no specific therapy. Symptomatic and supportive treatment:

- Haloperidol or phenothiazine for dyskinesia. Tetrabenazine may be given.
- Psychological support.
- Institutional care for dementia.
- Genetic counselling is essential.

TREMOR

Instruction by the examiner:

- Look at this patient. What are your findings (resting tremor)? What else do you want to examine? (See other signs of Parkinsonism).
- The patient has tremor. Now examine.

During examination of tremor, proceed as follows:

- If the tremor is present at rest: see abduction–adduction of thumb (pill-rolling movement), flexion–extension of fingers. Likely diagnosis is **Parkinsonism** (then examine for other signs of Parkinsonism).
- If no resting tremor: ask the patient to outstretch his/her hands in front. If tremor is present, it is called **action tremor**. Then examine according to suspicion (check for thyrotoxicosis, history of taking drugs and family history).
- If no resting tremor or no tremor with outstretched hands (though cerebellar tremor may be present in outstretched hand), then test for intention tremor (cerebellar lesion). If present, check for cerebellar signs.
- If still no tremor, see for flapping tremor.

Presentation of a Case: Case No. 1 (Resting Tremor):

- The patient has resting tremor involving the right hand, there is pill-rolling movement of thumb and index finger. Tremor is reduced by holding something.

My diagnosis is **Parkinsonian tremor** (for details, see ‘Parkinson’s disease’)

Q: What else do you like to see?

A: I would like to see other signs of Parkinsonism (such as rigidity, hypokinesia, gait).

Presentation of a Case: Case No. 2 (Action Tremor):

- There is tremor on outstretched hand, which reduces or disappears on rest.
- Mention other features according to suspicion of cause (e.g., thyrotoxicosis, cerebellar tremor).

My diagnosis is **Action tremor** (for details, see below).

READ THE FOLLOWING TOPICS IN RELATION TO TREMOR

Q: What is **tremor**?

A: It is the involuntary, oscillatory and rhythmical movement of one or more parts of the body due to alternate contraction of a group of muscles and their antagonists.

Q: What are the causes of tremor?**A:** As follows:

- Functional (anxiety, hysterical conversion reaction, nervousness).
- Endocrine (thyrotoxicosis, pheochromocytoma, hypoglycaemia).
- Parkinsonism.
- Cerebellar tremor (also called intention tremor).
- Benign essential tremor.
- Senile tremor.
- Drugs: Salbutamol and other β -agonist, phenothiazines, butyrophenones, methyl dopa, lithium intoxication, anticonvulsant (phenytoin, carbamazepine, sodium valproate), amphetamine, theophylline, caffeine.
- Alcohol (chronic alcoholism and alcohol withdrawal).
- Toxin (mercury, arsenic, lead).
- General paresis of insane (GPI).
- Flapping tremor.

Q: What are the types of tremor?**A:** 3 types:

- Resting tremor (typical of Parkinsonism).
- Action tremor or postural tremor (present on outstretched hands).
- Intention tremor.

According to the amplitude or nature, it may be:

- Fine.
- Coarse.

Q: What are the causes of action tremor?**A:** As follows:

- Anxiety.
- Thyrotoxicosis.
- Senile tremor.
- Benign essential tremor.
- Cerebellar tremor (increases near the target).
- Drugs (see above).
- Familial.
- Idiopathic (in many cases).

Q: What is intention tremor?

A: Tremor that comes on voluntary movement, but disappears on rest is called intention tremor. It is caused by cerebellar lesion due to any cause.

Q: What is the nature of tremor of GPI?

A: Tremor is usually present in the tongue, seen during protrusion, manifested as backward and forward movement of the tongue, called trombone tremor (other features of GPI are dementia, Argyll Robertson pupil and bilateral UMN lesion signs).

Q: What are the causes of fine and coarse tremor?**A:** As follows:

1. Causes of fine tremor:
 - Anxiety or nervousness.
 - Thyrotoxicosis.
 - Senile tremor.
 - Benign essential tremor.
 - Drugs (e.g., salbutamol, terbutaline).
 - Familial.
 - GPI.
2. Causes of coarse tremor:
 - Parkinsonism.
 - Intention tremor.
 - Flapping tremor (in hepatic pre-coma).
 - Wilson's disease.
 - Sometimes in senile tremor.

Q: What is benign essential tremor?

A: It is a familial tremor, inherited as autosomal dominant, usually present in outstretched hands and also when hands adopt a posture such as holding a glass or spoon. Occasionally, present at rest. Worse in upper limbs. Often, there is titubation or voice tremor (but not isolated). Other features are:

- Usually bilateral symmetrical tremor.
- Slowly progressive, rarely produces severe disability. No rigidity, no hypokinesia.
- Tremor is not aggravated by movement.
- It is common in elderly (but may occur at any age).
- Handwriting is shaky and untidy, but no micrographia.
- Anxiety increases the tremor.

Q: What is the site of lesion in benign essential tremor?

A: Patchy neuronal loss in cerebellum and cerebral connection.

Q: How to treat benign essential tremor?**A:** As follows:

- Propranolol is helpful in small dose.
- Alcohol may relieve the tremor but there is chance of addiction.
- Primidone is sometimes helpful.
- Rarely in severe cases, injection of botulinum toxin may be helpful.
- Surgery: in intractable cases, stereotactic thalamotomy or thalamic deep brain stimulation.

Q: What are the differences between benign essential tremor and Parkinsonian tremor?

A: (See in 'Parkinsonism').

SPEECH

Instruction by the examiner:

- 1. Instruction 1:** Talk to the patient or ask some questions to the patient (this is usually asked to test whether a candidate can diagnose the type of speech disorder by talking to the patient). Usual speech disorders are:
 - Dysarthria.
 - Dysphasia.
 - Dysphonia.
 - Any voice change: Husky and croaky (myxoedema).
- 2. Instruction 2** (other than speech disorder): Look at the patient. Now, ask some questions.

For instruction 1, proceed as follows:

- Once you talk to the patient, try to find out the nature of speech.
- Is it dysphasia, dysarthria or dysphonia?

Next question will be according to the nature of speech, as follows:

If it is dysarthria, ask some questions to find out the type of dysarthria:

- Ask a question with long sentence (e.g., 'Would you please tell me your name and address'? or 'What breakfast did you take this morning'?).
- Ask the patient to tell 'British constitution or West Registrar Street'. Ascertain whether the speech is cerebellar or pseudobulbar or bulbar palsy.
- Is it scanning or staccato? (Slow, slurred, explosive or speech broken into syllable-by-syllable. It is suggestive of cerebellar lesion).
- Is it spastic? (Pseudobulbar palsy).
- Is it nasal and indistinct? (Bulbar palsy).

If dysphasia, try to find which type of dysphasia (motor or sensory or nominal or global). See, whether comprehension is good or impaired:

- If comprehension is impaired: it is sensory type.
- If comprehension is good: it is expressive or motor type.

If the patient cannot answer or talk, then ask the following questions:

- What is your name?

If unable to answer, then ask:

- Close your eyes.
- Put out your tongue.
- Raise your right or left hand or both hands above head.

If the patient **can perform** all these, it is **motor type** of dysphasia.

If comprehension is not good: The patient answers fluently, but speech is meaningless or incoherent (not related with the question). There may be inappropriate words or new words or non-existing words. Hence, it is likely to be **sensory type** of dysphasia.

If the patient **neither answers nor responds** to your instructions, such as:

- What is your name? (no answer).
- What is your address? (no answer).

Then hold a pen in front of the patient. Ask him/her:

- 'What is it'? If no answer, then ask:
- 'Is it a key'? The patient answers, 'No'.
- 'Is it a pen'? The patient answers, 'Yes'.

Then the diagnosis is **nominal dysphasia** (the patient answers either **yes** or **no**).

Q: What are the component parts of speech?

A: 3 component parts of speech:

- Phonation (abnormality is called dysphonia).
- Articulation (abnormality is called dysarthria).
- Language (abnormality is called dysphasia).

Q: What is dysphasia?

A: It is the disordered use of language with or without impaired comprehension of received speech.

Q: What are the types of dysphasia?

A: 4 types:

- Motor dysphasia (expressive).
- Sensory dysphasia (receptive).
- Nominal dysphasia.
- Global dysphasia (both motor and sensory).

N.B.: For details about dysphasia, see in the topic 'Dysphasia' later in this chapter.

Q: What is dysarthria?

A: It means the defect in articulation and enunciation of speech. It may result from the lesion of the muscles, myoneural junctions or motor neuron of lips, tongue, palate and pharynx.

Q: What are the types of dysarthria?

A: As follows:

- Scanning (found in cerebellar lesion).
- Spastic (found in pseudobulbar palsy).
- Paralytic (found in bulbar palsy).
- Extrapyrimal (slow, slurred, monotonous, husky, dysphonia or aphonia).
- Variegated (found in hypothyroidism, multiple ulcer or thrush in the mouth, amyloidosis due to large tongue and temporomandibular arthritis).

Q: Where are the sites of lesion in different types of dysarthria?

A: As follows:

- UMN lesion of cranial nerves.
- Cerebellum.
- Brainstem.
- Extrapyrimal system.
- At the periphery in the muscles of face, lip, tongue and pharynx.

N.B.: For details about dysarthria, see in the topic 'Dysarthria' later in this chapter.

Q: What is **dysphonia**?

A: It is the alteration of quality of voice with reduction in volume as a result of vocal cord disease. It is a disorder of vocalization, the fault is in the vocal cord.

Q: What are the **causes of dysphonia**?

A: It is found in laryngitis, tumour of the vocal cord or bilateral adductor paralysis. Sometimes, hysterical.

For instruction 2 (by looking at the face):

Proceed as follows: There is likely to be obvious diagnosis by looking at the patient. Now talk to the patient to find out typical speech change in that particular disease. Examples are:

- Hypothyroidism—croaky or husky voice.
- Parkinsonism—slow initiation of voice, dysphonia.

Q: What is the **difference** between dysphasia and dysarthria?

A: Dysphasia is a disorder of language, but dysarthria is a disorder of speech.

Q: Which **cerebral hemisphere** is responsible for language function?

A: Dominant hemisphere. Left hemisphere is dominant in 97% right handed person and 50 to 60% left handed person.

DYSPHASIA

Instruction by the examiner:

- Talk to the patient. Or, ask some questions to this patient.

Presentation of a Case (Motor Dysphasia): Case No. 1

- The patient can understand, but is unable to talk or answer the questions.
- Or, the patient is unable to talk, but can talk a few words after sometime. There is lack of fluency, he/she has difficulty in finding some words, but comprehension is good.

My diagnosis is **Motor (expressive) dysphasia** (also called Broca's dysphasia).

Q: What else do you want to examine?

A: I want to examine to see any signs of hemiplegia, more likely right sided (ask the patient to raise his/her hands, legs. The patient is unable to do so). In a right-handed person, left hemisphere is dominant and it is also dominant in 50% of left handed person.

Q: Where is the site of lesion in motor dysphasia?

A: Broca's area (posterior part of inferior frontal gyrus), in dominant hemisphere (along the middle cerebral artery or of its frontal branch).

Q: What are the causes? How is the prognosis?

A: Cerebrovascular disease (such as cerebral infarction or haemorrhage). Prognosis is good.

Presentation of a Case (Sensory Dysphasia): Case No. 2

- The patient speaks fluently, but cannot understand the spoken (auditor dysphasia) or written word (alexia).
- Speech is unintelligible, which is incorrect word (e.g., hand for foot), inappropriate words (paraphasia, incorrect syllable in word e.g., tooth brush as tooth smooth, new words (neologism) and non-existing words (Jargon dysphasia).

My diagnosis is **Sensory (receptive) dysphasia**.

Q: What is the cause?

A: Cerebrovascular disease (such as infarction or haemorrhage). It may be also due to space occupying lesion.

Q: Where is the site of lesion?

A: Posterior part of dominant superior temporal gyrus (called Wernicke's area).

Q: What else do you like to examine in this patient?

A: I want to test for:

- Homonymous hemianopia.
- Sensory function (which are impaired or diminished on right side of the body).
- Dyslexia (difficulty in reading).
- Dysgraphia (difficulty in writing).
- Dyscalculia (difficulty in calculation).

Q: What **happens** in repetitive speech?

A: Severely impaired (it is better in expressive type).

Q: What is the **prognosis**?

A: Recovery is usually good.

Presentation of a Case (Nominal Dysphasia): Case No. 3

- The patient has difficulty in naming the object, but comprehension is good and the speech production is better.

My diagnosis is **Nominal dysphasia**.

Q: What is **Nominal dysphasia**?

A: It is a type of motor dysphasia in which there is difficulty in naming the familiar object (although naming difficulty may occur in all dysphasia), but other aspects of speech are normal. The patient usually talks less, answer is either 'yes' or 'no' and comprehension is good.

Q: Where is the **site of lesion** in nominal dysphasia?

A: Dominant posterior part of temporo-parietal area. It is rare in its pure form. Sometimes, the patient uses long sentences to overcome the failure to find the correct word (called circumlocution).

Presentation of a Case (Global Dysphasia): Case No. 4

- The patient has marked disturbance both in comprehension and in expression.

My diagnosis is **both Motor and Sensory (Global dysphasia)**.

Q: Where is the **site of lesion** in Global dysphasia?

A: Extension of infarction in the left cerebral hemisphere along the territory of left middle cerebral artery. The patient has difficulty in reading, writing and also there are:

- Right sided hemiplegia.
- Right homonymous hemianopia.
- Marked intellectual deterioration.

Q: How is the **prognosis**?

A: Prognosis is **poor**.

Presentation of a Case (Conductive Dysphasia): Case No. 5

- The patient speaks fluently, comprehension is good, but repetition is impaired and difficulty in naming the object.

My diagnosis is **Conductive dysphasia**.

Q: What is **conductive dysphasia**?

A: In this type of dysphasia, the patient follows the command, speaks fluently and comprehension is good, but repeating the statement is poor and naming the object is also poor.

Q: Where is the site of lesion?

A: Arcuate fibre or the fibres communicating between Wernicke and Broca area.

Q: What is angular gyrus syndrome?

A: If angular gyrus is affected in addition to nominal dysphasia, there are alexia (inability to read), dyslexia (difficulty in reading), agraphia (inability to write), dysgraphia (difficulty in writing). This is called Angular gyrus syndrome.

Q: What investigations should be done in a patient with dysphasia?

A: As follows:

- CT scan of head or MRI of brain.
- Blood sugar.
- Lipid profile.
- Cardiac-ECG, Echocardiogram.

DYSARTHRIA

Instruction by the examiner:

- Talk to the patient.

Presentation of a Case (Dysarthria): Case No. 1 (Cerebellar Type)—

- The patient has slow, slurred, scanning speech, explosive in nature.

My diagnosis is **Cerebellar speech (Scanning or Staccato)**.

Q: What **else** do you want to see?

A: Cerebellar signs (see cerebellar lesion).

Presentation of a Case (Bulbar Palsy): Case No. 2

- The speech is nasal, indistinct, slurred. There is (may be) dribbling of saliva.

My diagnosis is **Bulbar palsy**.

N.B.: For diagnosis of bulbar palsy, remember the 3 ‘Ds’ (Dysarthria, Dysphonia and Dysphagia).

Q: What **else** do you want to see?

A: As follows:

- Palate: Absent movement (ask the patient to say ‘aah’ and see the palate).
- Tongue: Wasting, wrinkled and fasciculation.
- Gag reflex: Absent.
- The patient has nasal regurgitation.

Q: What is the **site** of lesion in bulbar palsy?

A: Nucleus of lower cranial nerves in medulla (IX, X, XI and XII). Lesion is bilateral and LMN type.

Q: What are the **causes of bulbar palsy**?

A: As follows:

- Motor neuron disease.
- Guillain–Barré syndrome.
- Syringobulbia.
- Brainstem infarction.
- Poliomyelitis.
- Neurosyphilis.
- Neurosarcoïd.

Presentation of a Case (Pseudobulbar Palsy): Case No. 3

- The speech is indistinct, slurred and high pitched (so called **Donald Duck** or **Hot Potato** dysarthria due to tight immobile tongue).
- The tongue is spastic (small and tightened), unable to protrude.
- There is no wasting, no fasciculation.
- Palatal movement is absent.
- Gag reflex is present.
- Jaw jerk is exaggerated.
- The patient is emotionally labile (laughing or crying).

My diagnosis is **Pseudobulbar palsy**.

Q: Where is the **site of lesion** in pseudobulbar palsy?

A: Bilateral UMN lesion (supranuclear) involving pyramidal tract (supranuclear lesion of lower cranial nerves: IX, X, XI, XII).

Q: What **else** do you want to examine?

A: As follows:

- Sensory change (no abnormality).
- Signs of UMN lesion (bilateral generalized spasticity).
- Dysphagia.
- Aphonia or dysphonia (in severe cases).

Q: What are the **causes** of pseudobulbar palsy?

A: As follows:

- Bilateral repeated cerebrovascular disease involving internal capsule (multi-infarct dementia).
- Demyelinating disease (Multiple Sclerosis).
- Motor neuron disease.
- Others: Brainstem tumour, trauma.

Q: Why pseudobulbar palsy is **found** in bilateral lesions only?

A: Because most cranial nerve nuclei receive bilateral innervations from corticobulbar tract.

Q: What are the **differences** between bulbar and pseudobulbar palsy?

A: As follows:

Criteria	Bulbar Palsy	Pseudobulbar Palsy
1. Type of lesion	LMN	UMN
2. Site of lesion	Medulla	Bilateral, internal capsule
3. Speech	Nasal	Slow, slurred and indistinct
4. Nasal regurgitation	Present	Absent
5. Tongue	Wasted, fasciculation	Small, stiff or spastic
6. Jaw jerk	Absent	Brisk
7. Emotion	Normal	Labile

Q: What are the **structures involved** in articulation of speech and how to test?

A: As follows:

- Lips: ask the patient to say, 'me, me, me'.
- Tongue: ask the patient to say, 'la, la, la'.
- Pharynx: ask the patient to say, 'kuh, gut'
- Palate, larynx and expiratory muscles: ask the patient to say, 'ah'. In palatal paralysis, the patient's speech is worse when the head is bent forward.

Presentation of a Case (Hypokinetic dysarthria): Case No. 4

- The patient's speech is slow, monotonous, low volume and low pitched.

My diagnosis is **Hypokinetic dysarthria** (characteristics of Parkinson's disease).

Q: What is the **site of lesion**?

A: Unilateral or bilateral lesions of substantia nigra or its connection.

Q: What **else** do you like to examine?

A: I want to examine the other signs of Parkinsonism.

EXAMINATION OF HANDS (WASTING OF SMALL MUSCLES OF HANDS)

Instruction by the examiner:

- Look at the hands. What is the diagnosis?
- Examine the hands or examine the upper limb.

By looking, the obvious diagnoses may be possible (for details see 'Examination of Hands' in Chapter 1). In this chapter, wasting of small muscles of hands, related to neurological diseases, are described.

Presentation of a Case (Hand): Case No. 1

- There is generalized wasting of small muscles of hands involving the thenar, hypothenar and interossei muscles with dorsal guttering and claw hand (flexion of interphalangeal joints and extension of metacarpophalangeal joints).
- There are few fasciculations.
- No sensory abnormality.

My diagnosis is **Motor neuron disease, more likely progressive muscular atrophy** (for details, see in MND).

Q: Mention one **differential diagnosis**.

A: Motor neuropathy (due to any cause).

Presentation of Case No. 2

- As in Case no. 1 **plus** sensory abnormality (mention whether median, ulnar or both).

My differential diagnoses are (wasting of small muscles of hand with sensory loss):

- Peripheral neuropathy due to any cause.
- Cervical spondylosis.
- Cervical rib.
- Cervical cord compression (neurofibroma, meningioma).
- Leprosy.
- Syringomyelia (dissociated sensory loss and trophic changes in hand).

Q: What **else** do you want to examine?

A: I want to examine:

- Neck (for cervical spondylosis, cervical rib, supraclavicular bruit).
- Dissociated sensory loss for syringomyelia (for details see later).
- Thickening of nerve (at elbow): Leprosy.
- Trophic change, ulcer, gangrene, burn.

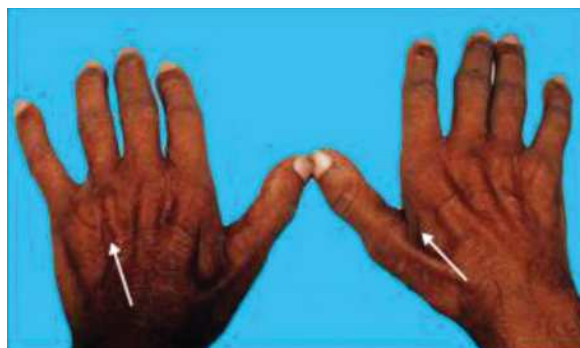
Q: What are the **causes** of wasting in one hand (unilateral)?

A: As follows:

- Cervical cord compression or cervical rib.
- Brachial plexus lesion (trauma, tumour).
- Pancoast tumour.
- Old poliomyelitis.
- Cerebral palsy.
- Leprosy.



Wasting of thenar and hypothenar



Wasting of dorsal interossei (guttering)

Q: What are the **causes** of wasting of small muscles of hand?

A: As follows:

- Motor neuron disease.
- Charcot–Marie–Tooth disease.
- Syringomyelia.
- Cervical spondylosis.
- Cervical cord compression.
- Cervical rib.
- Pancoast tumour.
- Peripheral nerve lesion (polyneuropathy, combined ulnar and median nerve lesion).
- Leprosy.
- Rheumatoid arthritis.
- Myopathy (dystrophia myotonica).

Presentation of a Case (Hand): Case No. 3

- There is flexion of interphalangeal joints and extension of metacarpophalangeal joints.

My diagnosis is **Claw hand**.

Q: What **else** do you like to see?

A: I want to see the ulnar nerve at elbow joint (may be thickened in leprosy).

Q: What is claw hand? What are the causes?

A: It is a deformity of hand characterized by flexion of all interphalangeal joints and hyperextension of metacarpophalangeal joints. It is due to weakness of lumbricals and interossei and unopposed action of long extensors of finger.

LMN lesions of C₈ and T₁ nerves, C₈ and T₁ nerve root lesion and brachial plexus lesion will produce localized wasting of lumbricals and interossei causing claw hand. A combined ulnar and median nerve lesion will produce true claw hand. Ulnar claw hand involves 4th and 5th fingers, because radial lumbricals are supplied by median nerve.

Causes of claw hand:

- Combined ulnar and median nerve lesion: Trauma, leprosy.
- Brachial plexus lesion (C₈ and T₁): Cervical rib, thoracic inlet syndrome, Klumpke's paralysis.
- Neurological disease: MND, Charcot–Marie–Tooth disease, syringomyelia, intramedullary tumour and polio.



Claw hand (dorsal surface)



Claw hand (palmar surface)



Ulnar claw hand

Claw hand-like deformity (pseudoclau hand) may occur in:

- Dupuytren's contracture. Volkmann's ischaemic contracture.
- Post-burn contracture.
- Diabetic cheiroarthropathy.

Presentation of a Case (Hand): Case No. 4

- There is generalized wasting of small muscles of hands with dorsal guttering.
- There are joint deformities (such as boutonniere, swan neck deformity, ulnar deviation).

My diagnosis is **Rheumatoid arthritis** (for details, see in the chapter musculoskeletal system).

SYRINGOMYELIA

Instruction by the examiner:

- Examine the hands or perform the neurological examination of the upper limbs.

Presentation of a Case:

- There is a scar mark or burn or painless ulcer on the index finger of right side (may be on other fingers).
- There is wasting of small muscles of hands and forearm, also dorsal guttering of hands is present. Few fasciculations are present (mention, if any).
- Joints: Hyperextension of MCP and flexion of interphalangeal joints giving rise to claw hand appearance.
- Muscle tone and muscle power are diminished.
- Biceps, triceps and supinator reflexes are diminished.
- There is dissociated sensory loss (loss of pain and temperature, but intact light touch, vibration and position sense) in the arms, shoulder and neck (classically in 'cape' distribution).

My diagnosis is **Syringomyelia**.

N.B.: To see vibration sense—test with tuning fork over the fingers, lower end of radius, elbow and clavicle.

Q: What **else** do you want to examine?

A: As follows:

- Eyes—for Horner's syndrome (indicates syringobulbia).
- Kyphoscoliosis, spina bifida and pes cavus.
- Charcot joints of shoulder and elbow.
- Examination of lower limbs (may be UMN lesion signs in lower limbs, spastic paraplegia).

N.B.: Look for any surgical scar mark in the neck (laminectomy for cervical spondylosis or syrinx decompression). Also, look for scar marks in shoulder (shoulder joint replacement).



Bilateral claw hand and wasting of small muscles of hands in syringomyelia



Hand wasting in syringomyelia



Scar with claw hand in syringomyelia



Callosities on dorsum of hand in syringomyelia

N.B.: Remember the following points:

- Trophic and vasomotor changes are common in syringomyelia.
- Painless scar and ulcers over the finger (due to loss of pain sensation).
- Callosities over the knuckles and thick skin (due to loss of pain sensation).
- Oedema and excessive sweating (central autonomic dysfunction).
- There may be amputation of digit.
- Classically there may be LMN lesion signs in upper limbs and UMN lesion signs in lower limbs.

READ THE FOLLOWING TOPICS IN RELATION TO SYRINGOMYELIA

Q: What is syringomyelia?

A: It is a developmental anomaly in which there are cavities filled with CSF surrounded by glial tissue near the centre of spinal cord, mostly originating at C8 and T1 segment, but may occur anywhere in the spinal cord. Expanding cavity may disrupt:

- Anterior horn cells of spinal cord.
- Lateral spinothalamic tract.
- Corticospinal tract.
- May extend upwards to involve brainstem (syringobulbia).

Q: What are the causes of syringomyelia?

A: As follows:

- Developmental anomaly (at the foramen magnum).
- Obstruction of 4th ventricle by congenital defect of the base of skull or cervical spine (Arnold–Chiari malformation).
- There may be arachnoiditis in the region of foramina of Magendie and foramina of Luschka.

Q: How the patient usually presents?

A: Presents in 3rd or 4th decade, rarely in early age, male and female are equally affected. The features are:

- Wasting of muscles of hands, forearms, shoulder girdles.
- Loss of pain and temperature sensation. Patient may complain of painless burn.
- Difficulty in walking.

Q: What are the physical findings in syringomyelia?

A: Triad of:

- Dissociated sensory loss in neck, shoulder and arm.
- LMN lesion signs in the upper limb (muscle atrophy and loss of reflex).
- UMN lesion signs in lower limbs.

Q: What investigations should be done?

A: As follows:

- X-ray of the neck (to see congenital anomaly of foramen and widening of cervical canal).
- MRI (investigation of choice) or CT scan.

Q: What are the CSF findings?

A: It may show high protein, which is higher in CSF blockage.

Q: How to treat syringomyelia?**A:** As follows:

- Supportive: Regular activity, physiotherapy, avoid burn, trauma or hot water.
- Surgical decompression may be necessary.

Q: What surgeries are possible?**A:** As follows:

- Cervical decompression: In which suboccipital craniectomy, C₁–C₃ laminectomy and duraplasty. This is done in Arnold–Chiari malformation.
- Dorsolateral myelotomy: In which syrinx is drained into the subarachnoid space, done after decompression.
- Shunt: Such as syringo-peritoneal shunt, syringo-subarachnoid shunt, ventriculo-peritoneal shunt.

Q: What are the features of syringobulbia?**A:** As follows:

- Dissociated sensory loss in the face.
- Horner's syndrome.
- Palatal palsy.
- Dysarthria.
- Nystagmus.
- Cranial nerve involvement (V, VII, IX and X).

Q: What is dissociated sensory loss? What are the causes?**A:** Loss of pain and temperature, but intact light touch, vibration and position sense.**Causes of dissociated sensory loss:**

1. Lesion at the centre of spinal cord (sensory loss is always bilateral and segmental). The causes are:
 - Syringomyelia (common).
 - Intramedullary neoplasm of spinal cord.
 - Haematomyelia.
2. Hemisection of spinal cord (Brown–Séquard syndrome).
3. Lesion at the anterior half of spinal cord: Anterior spinal artery occlusion (LMN lesion at the site and bilateral UMN lesion and lateral spinothalamic lesion below).
4. Lateral medullary syndrome: Thrombosis of posterior inferior cerebellar artery (PICA). Syringobulbia also produces same type of lesion.

MYOTONIC DYSTROPHY

Instruction by the examiner:

- Examine the hands. What else do you want to see?
- Look at the patient. What is your diagnosis? What else do you want to see?

During examination of myotonic dystrophy, proceed as follows:

- Look at the hands: Both front and back (apparently no abnormality).
- Tell the patient—'Close and open your hands repeatedly as quickly as possible'. The patient is unable to open the closed hands quickly (**myotonia**).
- Shake hands with the patient (the patient is unable to relax the hands—**grip myotonia**).
- Percuss on thenar eminence with your fingers (there are dimples or depressions that fill up slowly—**percussion myotonia**).
- Look at the face of the patient (signs in face—see below).
- Percussion may be done on tongue (dimples or depressions are seen).

Presentation of a Case (Hands): Case No. 1

- The patient is unable to open the hands after closing and also to relax the hands after handshaking due to myotonia.
- On percussion of thenar eminence, there are few dimples.

My diagnosis is **Myotonia**.

Q: What is the likely underlying disease?

A: Myotonia dystrophica.



Myotonia



Myotonia dystrophica



Neck muscle wasting

Q: What else would you like to see?

A: I want to examine the face, eye, upper limb, testes (see below).

Q: What is myotonia?

A: It is the continued contraction of muscles after cessation of voluntary contraction.

Presentation of a Case (by Looking at Face and Relevants): Case No. 2

1. In face:
 - Frontal baldness (the patient may be wearing wig).
 - Long, lean, triangular, sad and expressionless face.
 - Wasting of temporalis and masseter.
2. Eyes:
 - Partial ptosis (usually bilateral, may be unilateral) with smooth forehead.
 - Cataract (stellate cataract). May be posterior subcapsular fine deposit.
 - Difficulty in opening the eyes after firm closure.
3. Neck: Wasting of sternomastoid and shoulder girdle muscles. There is weakness of flexion and normal extension.
4. Others:
 - Wasting of distal muscles of arms (forearm wasting first) and legs.
 - Testes (atrophy).
 - Gynaecomastia.

My diagnosis is **Myotonic dystrophy**.

Q: What is myotonia dystrophica?

A: It is a genetic disorder, inherited as autosomal dominant characterized by failure to relax the muscle after forceful contraction. It is caused by trinucleotide repeat expansion in the myotonin protein kinase gene of chromosome 19q.

Q: What are the features of myotonia dystrophica?

A: Features as above plus:

- Inherited as autosomal dominant.
- Males are affected more than females.
- Age of onset may be any.
- Diabetes mellitus and impaired glucose tolerance (IGT) may occur.
- Intellect and personality may have mild deterioration.
- Small pituitary fossa and hypogonadism may occur.
- Low serum IgG levels
- Tolerate anaesthesia poorly.
- Heart (cardiomyopathy, valvular heart disease, mitral valve prolapse, arrhythmia or conduction defect).
- Oesophageal dysfunction, there may be dysphagia and aspiration.
- May cause repeated respiratory infection (due to low IgG).

Q: What do you mean by myopathic facies?

A: It is characterized by expressionless, sadlike facies with frontal baldness and ptosis. Sometimes, looks like sleepy appearance.

Q: What is the gait in myotonic dystrophy?

A: High steppage gait. Foot drop is present.

Q: What are the types of myotonic dystrophy?**A:** 2 types:

- Type 1: Classical type associated with distal muscular wasting and weakness.
- Type 2: Similar features, but there is proximal wasting and weakness.

Q: What are the EMG findings?**A:** High frequency activity that varies repeatedly to cause a characteristic sound on loud speaker (waxing and waning of potentials, called **Dive Bomber effect**).**Q: How to treat myotonia dystrophica?****A:** Only symptomatic. No specific treatment.

1. Myotonia may be treated by phenytoin (procainamide or quinidine may be used, but may worsen cardiac conduction).
2. Genetic counselling (the disease tends to be worse in successive generations).
3. Other symptomatic treatment:
 - Foot drop by special caliper.
 - For cardiac abnormality: pacemaker may be needed.

Q: Is prenatal diagnosis possible? How?**A:** Yes (if DMPK mutation identified in families). Done by:

- Chorionic villus sampling (at 10 to 12 weeks of gestation).
- Amniocentesis (after 14 weeks of gestation).

Q: What are the causes of myotonia?**A:** As follows:

- Myotonia dystrophica.
- Myotonia congenita.
- Others: Hyperkalaemic periodic paralysis, myxoedema (Hoffman's syndrome), hereditary paramyotonia (autosomal dominant), cold induced myotonia and drug (clofibrate).

Q: What is myotonia congenita? What is the prognosis and treatment?**A:** It is an inherited disorder (autosomal dominant), characterized by failure to relax the muscle after forceful contraction. Present at birth with feeding difficulty, inability to open the eyes and a peculiar cry. It is mild disease that improves with age. Other features of myotonia dystrophica are absent. There may be diffuse muscular hypertrophy due to continuous involuntary isometric contraction.**Prognosis:** Normal life expectancy.**Treatment:** Procainamide or quinidine may be helpful.

MYOPATHY (MUSCULAR DYSTROPHY)

Instruction by the examiner:

- Examine the upper limbs or lower limbs.
- Look at the face. What are your findings? Examine the relevants.

Presentation of a Case (Limb Girdle Myopathy): Case No. 1

- There is wasting of muscles of both upper limbs.
- Muscular weakness, mainly involving the proximal muscles (proximal myopathy).
- Muscle tone is normal.
- Patient has difficulty in standing from sitting (indicates proximal myopathy).
- Reflexes are normal or slightly reduced.
- No sensory abnormality.

My diagnosis is **Limb girdle myopathy**.



Limb girdle myopathy (front)



Limb girdle myopathy (back)



Difficulty in standing from sitting (proximal myopathy)

Q: What else do you want to see?

A: I want to examine the lower limbs (findings like upper limbs may be present).

Q: What is limb girdle myopathy?

A: It is a type of muscular dystrophy characterized by involvement of shoulder and pelvic girdle muscles.

- Type 1 (10%): Autosomal dominant, slower and later age of onset.
- Type 2 (90%): Autosomal recessive, occurs in childhood or early adulthood.
- Age of onset is 10 to 30 years, male and female are equally affected.
- May involve cardiac muscle (may cause conduction abnormality or heart failure).
- Calf pseudohypertrophy sometimes occurs.
- Face and hands are spared.
- Intelligence is normal.
- Muscle enzymes are normal or moderately elevated.
- Prognosis is poor, chair bound at 20 to 25 years of age (10 to 20 years after the onset of disease).

Presentation of a Case (Facio–Scapulo–Humeral Dystrophy): Case No. 2

- There is wasting of muscles of face, neck and shoulder girdle.
- Face looks dull, expressionless. Lips are open and slack. Also, inability to whistle and puff the cheek.
- Eyes: difficulty in closing the eyes (bilateral partial ptosis).
- Winging of scapula (due to involvement of serratus anterior muscle).
- Pectoralis and trapezius muscles are also wasted.
- Reflexes are normal or slightly reduced.
- No sensory abnormality.

My diagnosis is **Facio-scapulo-humeral dystrophy**.

Q: What is facio–scapulo–humeral dystrophy? What are the features?

A: It is a type of muscular dystrophy, inherited as autosomal dominant, characterized by involvement of muscles of face and shoulder girdle.

- Onset is 10 to 40 years of age. Course is variable, but usually relatively benign.
- There is wasting of muscles of face, neck and shoulder girdle (lower trapezzi, pectoralis, biceps, triceps). Hypertrophy of deltoid may occur.
- Winging of scapula (due to the involvement of serratus anterior muscle).
- Pain in shoulder girdle is common.
- Face looks dull, expressionless, lips open and slack. There is also inability to whistle and puff the cheek.
- Eyes: Bilateral partial ptosis. Fundoscopy shows retinal telangiectasia in 60% cases.
- Lower limb muscles are affected in 50% cases, usually at later age with weakness. Then foot drop occurs.
- Lower abdominal muscles are involved with sparing of upper abdominal muscles (Beever's sign—ask the patient to lie flat, then ask him to raise the head. This results in contraction of upper abdominal muscles with displacement of umbilicus upwards).
- Deafness may be present, intelligence is normal.
- Prognosis: Normal life span and slowly progressive.
- Muscle enzymes are usually normal or moderately elevated.
- Inflammatory and perivascular inflammation in muscle biopsy. Retinal microvascular abnormality may be found.



Facio–scapulo–humeral dystrophy



Winging of scapula



Pseudohypertrophy of calf muscles

Presentation of a Case (Duchenne Muscular Dystrophy): Case No. 3 (Young Male, Mention if Patient is Wheelchair Bound).

- There is pseudohypertrophy of calf muscles with wasting and weakness of lower limb muscles, also there is contracture of lower limbs.
- Proximal myopathy is present, involving the lower limb. Weakness and wasting of muscles of buttock are present.
- Wasting and weakness of the muscles of upper limb are also present (deltoid, infraspinatus).
- Neck flexors are more affected than extensor. Wrist extensors are more affected than flexors.
- Deep tendon reflexes are reduced (due to weakness of muscles).
- Face is normal.
- Kyphoscoliosis is present, gait may be waddling in early stage.

My diagnosis is **Duchenne muscular dystrophy**.

Causes of **pseudohypertrophy** of calf muscles:

- Duchenne muscular dystrophy.
- Becker's muscular dystrophy.

Presentation of a Case (Becker's Muscular Dystrophy): Case No. 4 (Young Male, Patient is Ambulant)

- There is pseudohypertrophy of calf muscles with wasting and weakness of upper and lower limb muscles.
- Proximal myopathy is present, involving the lower limbs.
- Face is normal.
- Gait: waddling gait.

My diagnosis is **Becker's muscular dystrophy**.

Q: What is Duchenne muscular dystrophy (DMD)?

A: It is a muscular dystrophy, inherited as X-linked recessive disorder (30% spontaneous mutation). Duchenne gene is on short arm of X-chromosome, Xp21 and its product called dystrophin is absent (diagnosed by western blot analysis of muscle biopsy).

Q: What are the features of DMD?

A: As follows:

- Affects only male, age of onset is 3 to 4 years.
- The child presents with difficulty in walking or getting up from sitting or lying position. There is history of frequent fall and delayed motor activity (e.g., walking).
- Gower sign is positive (while the child gets up from lying position, he uses the hands to climb up).
- There is pseudohypertrophy involving calf and deltoid muscles in early stage. Later, there is weakness, first involves the proximal muscles.
- Gait: Waddling (duck like).
- Other features: dilated cardiomyopathy, kyphoscoliosis, mental retardation. Respiratory involvement is early feature.
- Prognosis is poor, chair bound by the age of 10 years and few survive up to 20 years.
- Causes of death: dilated cardiomyopathy and respiratory failure or inanition.

Q: What is Becker's muscular dystrophy? What are the features?

A: It is a muscular dystrophy, inherited as X-linked recessive disorder, only males are affected and features are same as Duchenne type with the exception of:

- Onset is late (5 to 25 years).
- Less severe, less rapid progression and less cardiomyopathy. Mental retardation and kyphoscoliosis are uncommon. Respiratory involvement is a late feature.
- Chair bound at about 25 years after the onset, survival up to 4th to 5th decade.

Q: What is myopathy?

A: It is the disease of skeletal (voluntary) muscles, without neurological involvement.

Q: What is muscular dystrophy? What are the types of muscular dystrophy?

A: It is a group of hereditary muscular disorder characterized by progressive degeneration of groups of muscles without involvement of nervous system. There is absence or reduced dystrophin.

Types are:

1. Hereditary muscular dystrophy:
 - Duchenne type (pseudohypertrophic).
 - Becker's muscular dystrophy.
 - Limb girdle myopathy.
 - Facio-scapulo-humeral dystrophy.
 - Myotonia dystrophica.
 - Myotonia congenita.
 - Others: oculo-pharyngeal or ocular myopathy, congenital muscular dystrophy.
2. Congenital myopathy (rare):
 - Central core.
 - Nemaline myopathy.
 - Myotubular myopathy.
3. Secondary myopathy (due to endocrine disease and drugs).

Q: What investigations should be done in myopathy?

A: As follows:

- Serum CPK: very high, up to 100 to 200 times in Duchenne type (in other types, moderately raised).
- EMG shows short duration, low amplitude, spiky polyphasic action potential (spontaneous fibrillation is also seen occasionally), reduction in motor unit amplitude and duration with normal number of units activated during effort.
- ECG (shows cardiomyopathy and dysrhythmia), echocardiography.
- Blood sugar.
- Muscle biopsy (shows variation of muscle fibre size, degenerative changes, regeneration and replacement by fat. Immunological staining shows absence of dystrophin. This is commonly found in Duchenne muscular dystrophy).
- Lactic acid (to exclude mitochondrial myopathy).
- Molecular genetic testing.

N.B.: Remember the following points:

- Reflexes are reduced and later, absent (due to loss of muscle fibres), but ankle jerk remain intact even in late stage.
- Patient's cough is poor due to involvement of thoracic muscles.
- All myopathies involve proximal muscles (except myotonia dystrophica, which involves distal muscles).
- Myopathic facies means dull, expressionless, sad-like face. Found in myotonic dystrophy and facio-scapulo-humeral myopathy (normal in other myopathies).
- Fronto-temporal baldness indicates myotonic dystrophy.

Q: What are the difference between Duchenne and Becker's muscular dystrophy?**A:** As follows:

Points	Duchenne Muscular Dystrophy (DMD)	Becker's Muscular Dystrophy (BMD)
1. Age	Early onset (3 to 4 years)	Late (5 to 25 years)
2. Weakness	More severe	Less severe
3. Contracture	Early	Late
4. Kyphoscoliosis	Early	Late
5. Calf pseudohypertrophy	More prominent	Mild
6. Prognosis	Worse, early chair bound, survival up to 20 years.	Better, survival longer, up to 40 to 50 years.

Q: How to treat DMD and BMD?**A:** As follows:

- No specific treatment, only symptomatic and supportive treatment.
- Steroid may help to decrease the progression of disease.
- For cardiac abnormalities: anti-arrhythmic, even pacemaker may be needed.
- Non-invasive ventilation may be needed in advanced case.
- Physiotherapy and palliative care.
- Genetic counselling.

N.B.: Remember the following points:

- Prenatal diagnosis is possible.
- Diagnosis in female carrier is possible by high CPK in 70%, abnormal EMG and change in muscle biopsy.

Q: What is neuropathy and myopathy?**A:** As follows:

- Myopathy involves proximal muscles (except myotonia dystrophica, which involves distal muscles).
- Neuropathy involves distal muscles (except diabetic amyotrophy, GBS, amyloidosis, Lyme disease).

Q: What are the **difference** between neuropathy and myopathy?

A: As follows:

Points	Neuropathy	Myopathy
1. Distribution of weakness	Usually distal	Usually proximal
2. Reflexes	Usually lost early	Preserved till late
3. Sensory loss	Usually present	Absent
4. Contracture	Absent	Usually present
5. Atrophy	Present	Absent until late
6. CPK	Normal	Raised
7. NCV	Usually decreased	Normal
8. EMG	Fibrillations and fasciculations	Small motor units
9. Muscle biopsy	Group atrophy	Irregular, necrotic fibre

CARPAL TUNNEL SYNDROME (MEDIAN NERVE PALSY)

Instruction by the examiner:

- Examine the hands, **Or** look at the hands. What are your findings?

During examination of carpal tunnel syndrome, proceed as follows:

- Look at the palm (wasting of thenar muscles).
- Perform sensory test (loss of sensation along lateral three and half fingers).
- Motor functions: Examine the thumb (weakness of abduction, flexion and opposition of thumb) and also examine for interossei.
 - Pen touching test (to assess the weakness of abductor pollicis brevis): Ask the patient to lay the hand flat with palm upward. Ask to abduct the thumb vertically to touch the pen held above it. It is impossible, if median nerve palsy.
- Elicit the following signs:
 - Tinel sign: Percussion over the flexor aspect of wrist (flexor retinaculum) or tap the median nerve in forearm, the patient may experience paraesthesia along the distribution of the nerve.
 - Phalen sign: Flexion or extension of the wrist for 60 seconds produces paraesthesia along the distribution of nerve (lateral three-and-half fingers).
 - Tourniquet test: Raise BP above systolic for 120 seconds (produces paraesthesia).
 - Durkan test: Direct pressure over carpal tunnel for 30 seconds may produce paraesthesia.
 - Closed fist test: Flexion of fingers into a closed fist for 60 seconds produce paraesthesia in median nerve distribution.

Presentation of a Case:

- There is wasting of thenar muscles also weakness of abduction, flexion and opposition of thumb and weakness of lateral two lumbricals.
- Loss of sensation along the radial three-and-half fingers.

My diagnosis is **Carpal tunnel syndrome**.

Q: What else do you want to see?

A: I want to see the evidence of primary cause (see below).



Cutaneous supply in hand



Carpal tunnel syndrome (left hand)



Carpal tunnel syndrome (bilateral)

Q: What is entrapment neuropathy?

A: It is the neuropathy that occurs due to compression of a nerve while passing through an anatomical canal.

Q: What are the nerves involved in entrapment neuropathy?

A: As follows:

- Median nerve (at wrist).
- Ulnar nerve (at elbow or at wrist in Guyon's canal, which is bounded proximally by pisiform bone and distally by the hook of the Hammett).
- Radial nerve (at spiral groove of humerus).
- Meralgia paraesthetica (at inguinal ligament).
- Common peroneal nerve or lateral popliteal nerve (at the neck of fibula).
- Tarsal tunnel syndrome (at the flexor retinaculum at ankle joint, there is compression of posterior tibial nerve).

N.B.: In entrapment neuropathy, there is demyelination and may be axonal degeneration.

Q: What is carpal tunnel syndrome? What are the causes?

A: It is a type of entrapment neuropathy due to compression of median nerve under thickened flexor retinaculum of wrist causing wasting, tingling, numbness and pain along the distribution of the median nerve. Common in female (9%), less in male (0.6%).

Causes of carpal tunnel syndrome:

- Pregnancy (due to fluid retention, usually in the third trimester).
- Obesity.
- Rheumatoid Arthritis.
- Acromegaly.
- Myxoedema.
- CKD on long term dialysis (due to deposition of β_2 microglobulin, an amyloid).
- Tuberculous tenosynovitis.
- Primary amyloidosis.
- Tophaceous gout.
- Drug (oral contraceptive pill).
- Osteoarthritis of carpus (related to old fracture).
- Idiopathic (common in female, middle aged and obese. May occur in male with unaccustomed hand use, e.g., house painting).

Q: What is the usual presentation of carpal tunnel syndrome?

A: Nocturnal pain, numbness and paraesthesia in the palm and fingers often occurs at night, awakening the patient from sleep. Pain may be referred to the whole arm and shoulder.

Q: How to confirm the diagnosis?

A: By nerve conduction study.

Q: How to treat?**A:** As follows:

- Treatment of primary cause.
- Splint in wrist, especially at night, local steroid injection (in intracarpal tunnel) and diuretic may help.
- In severe cases: Surgical decompression of carpal tunnel may be required.

Q: What is meralgia paraesthetica?

A: It is a type of entrapment neuropathy due to compression of lateral cutaneous nerve of thigh on leaving the pelvis, just medial to the anterior superior iliac spine. There is pain and paraesthesia over the upper and outer thigh with reduction of sensation. It is usually self limiting. Occasionally, may be treated with corticosteroid and local anaesthetic injection at the anterior superior iliac spine.

Causes are:

- Obesity.
- Pregnancy.
- Diabetes mellitus.
- Idiopathic.
- May be tight jeans.

Q: What are the muscles supplied by the median nerve in hand?**A:** As follows:**Muscles supplied by median nerve, mnemonic: LOAF**

- **L:** Lateral two lumbricals.
- **O:** Opponens pollicis.
- **A:** Abductor pollicis brevis.
- **F:** Flexor pollicis brevis.

***N.B.:** Median Nerve (C_6 - T_1) contains motor supply to all the muscles in the front of forearm except flexor carpi ulnaris and ulnar half of flexor digitorum profundus. Also small muscles of hand (LOAF)*

ULNAR NERVE PALSY

Instruction by the examiner:

- Examine the hands or look at the hands. What are your findings? What else do you want to do?

During examination of Ulnar nerve palsy, proceed as follows:

1. Look at palmar and dorsal aspect of hands. If generalized wasting, perform the neurological examination of hands.
2. To find out causes:
 - Evidence of fracture or dislocation of the elbow (injury, any scar or deformity).
 - Evidence of osteoarthritis at elbow.
 - Injury at the wrist or palm.
 - Thickened nerve.
 - Any causes of mononeuritis multiplex.

Presentation of a Case: (Supposing Right Side):

- There is generalized wasting of the small muscles of hands (except thenar) with dorsal guttering.
- Ulnar claw hand (extension of MCP and flexion of IP joint of 4th and 5th fingers).
- Loss of sensation along fifth and half of the fourth finger (involving both palmar and dorsal surface).
- There is weakness of abduction and adduction of fingers with wasting of the medial side of forearm (due to involvement of flexor carpi ulnaris and medial half of flexor digitorum profundus).
- Froment's sign is positive.
- There is no weakness of wrist flexion.

My diagnosis is **Ulnar nerve palsy**.

Q: What are the **causes** of ulnar nerve palsy?

A: As follows:

1. At elbow:

- Fracture of ulna or dislocation of elbow.
- Osteoarthritis of elbow.
- Compression by fibrous arch of flexor carpi ulnaris.
- Compression during general anaesthesia.

2. At wrist:

- Injury or fracture at the wrist or palm.
- Ganglion, tumour.

3. Occupation:

With constant leaning of elbows (clerk) or constant flexion or extension at elbow (carpenter, painter, decorator) and wrist (screw driver, drills).

4. Mononeuritis multiplex due to any cause (DM, PAN, RA, SLE, amyloidosis and leprosy).

Q: What are the **motor and sensory** supplies of ulnar nerve (C₈ and T₁)?

A: As follows:

- Motor supply to small muscles of hand (except LOAF), flexor carpi ulnaris and medial half of flexor digitorum profundus.
- Sensory supply to the 5th finger and half of the 4th finger.

N.B.: *Remember the following points:*

- *Muscles of thenar eminence are supplied by median nerve.*
- *1st and 2nd lumbricals are supplied by median nerve.*
- *3rd and 4th lumbricals and interossei are supplied by ulnar nerve.*

RADIAL NERVE PALSY

Instruction by the examiner:

- Examine the hands or look at the hands. What are your findings? What else do you want to do?

During examination of radial nerve palsy, proceed as follows:

1. Ask the patient:
 - To raise both arms in front (obvious wrist drop).
 - To extend the wrist (weakness of wrist extension).
 - To extend the elbow against resistance—weakness of elbow extension (due to triceps involvement).
2. Test for brachioradialis: Ask to flex the elbow with forearm halfway between pronation and supination (there is failure to flex, brachioradialis does not spring up).
3. Pronation and supination (impaired).
4. The patient is unable to straighten the fingers. However, if the wrist is passively extended, the patient is able to straighten fingers at IP joints (due to action of interossei and lumbricals), but is unable to extend MCP joints.
5. Grasp is weak, but improves if wrist is extended.
6. Check sensation over the anatomical snuff box for dorsal aspect of thumb (there is loss of sensation).
7. Triceps reflex (absent).

Presentation of a Case: (Supposing Right Side):

- There is wrist drop on the right side,
- Weakness of wrist and elbow extension.
- Patient is unable to extend the fingers but when the wrist is extended, finger extension is normal.
- Grip is weak on right side but improvement with extended wrist.
- Finger abduction–adduction is impaired but can do when the hand is kept flat on table with extended fingers.
- There is sensory loss over the anatomical snuff box on right side.
- Triceps reflex is absent on right side.

My diagnosis is **Radial nerve palsy**.

Q: What are the causes of radial nerve palsy?

A: According to the site:

- Axilla: Trauma, radiation, compression by improper use of crutch, axillary growth.
- Spiral groove or mid shaft of humerus: Trauma, compression (e.g., Saturday night palsy).
- Proximal forearm: Trauma, subluxation of radius, repetitive forearm supination.
- Wrist: Trauma, compression by tight bracelet or handcuff.
- Chronic lead poisoning.
- Mononeuritis multiplex (due to any cause).

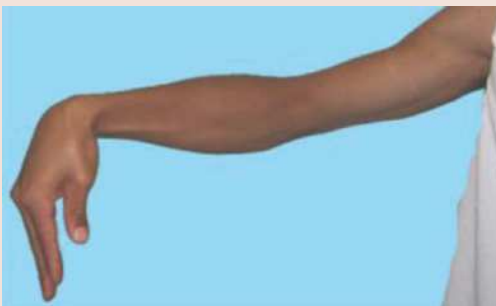
Q: What is Saturday night palsy?

A: In this disorder, the patient is heavily sedated with alcohol, sleeps with the arms hanging over the back of chair. As a result, radial nerve is compressed at the middle third of humerus causing paralysis of the nerve. Brachioradialis, supinator and extensors of forearm are involved. Usually, complete recovery occurs within weeks.

N.B.: Radial nerve is vulnerable to be involved at 4 sites:

- Axilla (incorrect use of crutch).
- Spiral groove of humerus (mid-shaft fracture and Saturday night palsy).
- Damage to the posterior interosseous nerve at proximal forearm, where it penetrates the supinator muscle.
- Sensory branch may be compressed at the wrist.

Anatomy of radial nerve: It is the termination of posterior cord of brachial plexus, derived from C₅₋₈ and T₁ spinal nerve. In elbow, it gives 2 branches—superficial radial (entirely sensory) and posterior interosseous (entirely muscular). It gives motor supply to brachioradialis, supinator and extensors of the forearm.



Wrist drop

CRANIAL NERVES

Instruction by the examiner:

- Examine the cranial nerves. (Remember, the examiner may stop you at any point and you must be ready to answer).

During examination of cranial nerves, proceed as follows:

- Ask the patient to sit at the edge of bed, face to face. See any obvious finding (ptosis, squint, asymmetry of face and dribbling of saliva).
- Now examine the individual cranial nerve as follows:

FIRST CRANIAL NERVE:

- Examine the nose quickly with a torch light to see any deviated nasal septum (DNS), polyp.
- Ask the patient, 'Do you have any difficulty in your sense of smell'? (Ideally use a perfume, put in each nostril and ask, 'Do you get the smell'?).

SECOND CRANIAL NERVE:

- Acuity of vision.
- Colour vision.
- Field of vision.
- Fundoscopy (should be done at the end).

Ask the patient whether he uses any glass. If so, ask to wear it and do the examination (each eye should be examined separately).

Acuity of vision (examine both distant and near vision): Better use a Snellen's chart (a mini Snellen's chart may be used). If not available, proceed as follows:

- Distant vision: Ask the patient, 'Look at the wall clock. What is the time now'? 'Look at the window. How many rods are there in the window'?
- Near vision: Ask, 'Read the newspaper or look at any small object'.

Colour vision (ideally it should be done with Ishihara chart):

- Show different colours to the patient and ask, 'What colour is it'?

Field of vision (Sit opposite to the patient, 1 metre apart at a same plane. Test each eye separately):

- To examine the right eye, ask the patient, 'Cover your left eye with left hand gently, look steadily at my left eye' (you should cover your right eye). No one should move the eye and should look each other's tip of the nose.
- Hold your index finger midway and from periphery, bring towards the centre until you see it. Ask the patient, 'Do you see my finger? Tell me when you see it.'
- If the patient fails to see, continue to bring the finger and ask when the patient can see.
- In this way, see in horizontal, upper and lower quadrant (temporal field).
- Then, see nasal field in the same way.
- Change your hand and repeat in other eye in the same manner.

Test of central scotoma:

- Use a red headed pin, move it from temporal side to nasal side in the midway. Ask the patient, 'Do you see it? Tell me, when it disappears'.

Finally perform fundoscopy (see in Chapter 10, 'Examination of the Eye').

IIIrd, IVth AND VIth CRANIAL NERVES:

- Look for any obvious ptosis and squint. Next examine eye movement.
- Ask the patient, 'Look at my finger. Follow it with your eyes with head fixed'.
- See movements in horizontal and vertical directions like the pattern 'H'.
- See any **nystagmus**. At extreme gaze, ask, 'Do you see one or two fingers (diplopia)'?
- Next examine pupil: Size, shape, light and accommodation reflex (see in Chapter 10, 'Examination of the Eye').

If diplopia is present, further test is necessary as follows:

- Ask to describe false image (it is pale, less distinct and more peripheral than real one). Ask, 'Whether two images lie side by side or one above the other'.
- If images are side by side, it indicates medial or lateral rectus palsy. If images lie one above the other, then either oblique muscles or superior or inferior recti are involved.
- To decide which pair of muscles are responsible, ask, 'In which direction, there is maximum image separation?' (Separation is greatest in the direction in which the weak muscle has its purest action).
- Now at the point of maximum separation, cover one eye and find which image disappears. Loss of lateral image indicates that covered eye is responsible.
- If diplopia persists after covering one eye, it may be due to astigmatism, dislocated lens or con-version disorder.

Vth CRANIAL NERVE: Perform both motor and sensory tests:**Motor test** (see any wasting of masseter and temporalis muscles):

- Ask the patient, 'Clench your teeth tightly.' Palpate the muscles.
- Test for pterygoids: Ask the patient, 'Open your mouth and stop me from closing it' (if paralysis is on one side, muscle of that side is less prominent and jaw deviates towards the side of lesion).
- Test for jaw jerk.

Sensory test: Test along the 3 divisions of nerve on each side using cotton and pin with eye closed. Test corneal reflex with wisp of cotton. Touch the cornea (not conjunctiva), see if there is reflex blinking.

N.B.: Remember the following points:

- *Corneal reflex: Afferent (sensory) passes through ophthalmic division of Vth nerve and efferent (motor) through VIIth nerve.*
- *If blinking on contralateral eye, but absent in tested eye, it indicates VIIth nerve lesion in ipsilateral eye (eye tested). Only one or three divisions of Vth nerve may be lost:*
 - *If all sensory are lost, then lesion in ganglia or sensory root (as in acoustic neuroma).*
 - *If only one branch of sensory is lost, then lesion is preganglionic.*
 - *If dissociated sensory loss in face, then lesion in brainstem or upper cervical cord (due to occlusion of posterior inferior cerebellar artery).*

VIIth CRANIAL NERVE: Perform motor and sensory tests. Look at face and see the following (found in VIIth nerve palsy):

- Obvious facial asymmetry, affected eye appears open and wide.
- Unilateral drooping of the corners of mouth.
- Nasolabial fold is less pronounced.

Motor test:

- Tell the patient, 'Look at the ceiling, keep head fixed'. See wrinkling of forehead, if absent wrinkling—whether unilateral or bilateral (it is the test for frontal belly of occipitofrontalis).
- 'Close your eyes tightly, do not let me open' (it is the test for orbicularis oculi). If it fails to close, look for Bell's phenomenon.
- 'Ask to whistle' (it is the test for orbicularis oris).
- 'Puff your cheek out' (it is the test for buccinator). If paralysis, air escapes easily on the affected side.
- 'Show me your teeth and have a smile' (it is the test for levator anguli oris and risorius). If paralysis is present, face is drawn to the healthy side.

Sensory test:

- Taste sensation in anterior two-thirds of tongue (nerve fibres pass along the lingual nerve to chorda tympani, then to geniculate ganglion of facial nerve and then to medulla oblongata).
- Posterior one-third of tongue is through glossopharyngeal nerve.

Finally, look at external auditory meatus and palate to see rash (found in Ramsay Hunt's syndrome). Also, test for hyperacusis (nerve to the stapedius muscle).

VIIIth CRANIAL NERVE:

Vestibular division:

- Ask the patient about any vertigo or dizziness or giddiness.

Cochlear division:

- Look at the external ear and meatus (wax and rash).
- Rub your finger or keep watch near ear, ask the patient, 'Can you hear it'?
- 'Rinne test' and 'Weber test' may be necessary (normally, air conduction is better than bone conduction).

IXth AND Xth CRANIAL NERVES:

- While talking to the patient, observe any nasal voice or hoarseness (hoarseness indicates bilateral paralysis of superior laryngeal branch of vagus). If it is unilateral, then it is usually asymptomatic.
- Ask the patient about any nasal regurgitation.
- 'Open your mouth and say aah': See palatal movement (arching of palate). If one side remains flat and immobile, it indicates paralysis of that side (soft palate is pulled to the normal side).
- Ask to cough: If bovine cough, indicates recurrent laryngeal nerve palsy.
- Palatal reflex (gag reflex, IXth nerve): Touch back of pharynx and see constriction.
- Taste sensation in posterior one-third of tongue (IXth nerve).

XIth CRANIAL NERVE:

- Ask the patient, 'Shrug your shoulder against resistance' (trapezius muscle).
- 'Turn your head to the other side against resistance, feel sternocleidomastoid' (test on both sides).

XIIth CRANIAL NERVE:

Look at the tongue to see any:

- Wasting.
- Fasciculation.
- Small and spastic or tight.

Ask the patient: 'Put out your tongue'. Observe the following:

- If small and spastic (unable to protrude).
- Deviation (towards the weak side).

Ask the patient, 'Waggle your tongue'. Feel the weak side.

N.B.: Remember the following points:

- *In unilateral UMN lesion, there may not be any change in tongue.*
- *In bilateral UMN lesion, tongue is small, spastic and unable to protrude (found in pseudobulbar palsy, IXth, Xth and XIIth cranial nerve palsy).*
- *In LMN type of lesion, there is wasting, fasciculation and weakness of tongue (found in bulbar palsy, IXth, Xth and XIIth cranial nerve palsy).*

FACIAL (VIITH) NERVE PALSY

Instruction by the examiner:

- Look at the face. What are your findings? What else do you want to examine?
- Examine the face.
- Examine the facial nerve.

Presentation of Case No. 1 (Instruction 1, by Looking Face, Supposing Left Side):

- Facial asymmetry.
- Drooping of the left corner of mouth.
- Left eye appears wide and open.
- Nasolabial fold: Less pronounced.

Q: What else do you want to examine?

A: I want to examine VIIth cranial nerve.

Presentation of Case No. 2 (Instruction 2 or 3, Supposing Left Side):

- Facial asymmetry.
- There is failure of wrinkling of forehead on left side.
- The left eye cannot be closed. On attempting to close, Bell's phenomenon is present (eyeball is rolled upwards and outwards).
- On puffing the cheek, there is weakness of left side of face.
- Failure to whistle and smile.
- While showing the teeth, lips are drawn to right side.

My diagnosis is **Left sided Bell's palsy**.

Q: Why it is Bell's palsy?

A: Because Bell's phenomenon is present along with facial palsy.



Failure of wrinkling of forehead (left)



Left eye—wide and open



Showing teeth (lips drawn to right)



Failure to whistle

Q: What else do you want to examine?

A: As follows:

- Taste sensation in anterior 2/3rd of tongue (to see chorda tympani).
- Palate and external auditory meatus to see any vesicle (found in Ramsay Hunt's syndrome).
- Evidence of hyperacusis.

Q: What is Bell's palsy?

A: It is a LMN type of facial palsy associated with Bell's phenomenon.

Q: What are the causes of Bell's palsy?

A: Idiopathic in 95% cases. It may be related to viral infection, due to reactivation of latent herpes simplex virus I.

Q: Where is the site of lesion in Bell's palsy?

A: Facial canal, in petrous part of temporal bone (in stylomastoid foramen).

Q: What is Bell's phenomenon?

A: On attempting to close the eyes, the eyeball rolls upwards and outwards, which is called Bell's phenomenon. It is a normal phenomenon, but cannot be seen because eyes are closed normally. It is only seen in Bell's palsy.



Left-sided Bell palsy
(Bell phenomenon)



Bilateral Bell palsy (Bell
phenomenon in both eyes)



Right sided facial palsy



Rash in ear in Ramsay
Hunt's syndrome

Q: What is the relation between diabetes mellitus and Bell's palsy?

A: Diabetes mellitus is thought to be responsible for 10% cases of Bell's palsy.

Q: What are muscles tested in Bell's palsy?

A: As follows:

- Frontal belly of occipitofrontalis (wrinkling of forehead).
- Orbicularis oculi (closes of eyes).
- Corrugator supercilii (frowning).
- Buccinator (puffing of cheek).
- Orbicularis oris (whistling).
- Levator anguli oris and risorius (showing the teeth and smiling).
- Stapedius muscle (hyperacusis).

Q: How to treat Bell's palsy?**A:** As follows:

- Prednisolone 60 mg daily for 5 days, should be tapered over next 5 days. It should be given within 72 hours.
- In severe case, prednisolone plus antiviral: may be given within 72 hours: Acyclovir 400 mg 5 times daily for 7 days or valacyclovir (500 mg twice daily for 5 to 7 days)
- Physiotherapy: Facial exercise and electro-stimulation within 14 days.
- Protection of eye during sleep (shut with tape, or even tarsorrhaphy), artificial tears or ointment.
- Residual paralysis may occur in 10% cases. Cosmetic surgery may be helpful.

During recovery, aberrant reinnervation may occur producing unwanted facial movement and tear during salivation (called **crocodile tear**).

Q: What is the prognosis of Bell's palsy?**A:** As follows:

- Spontaneous improvement begins in 2nd week, 70 to 80% cure within 12 weeks. May take 12 months. Less than 10% may have residual weakness.
- Prognosis can be detected by EMG: Reduction of amplitude of facial muscle action potential in 1st week indicates slow or incomplete recovery.

Q: What is Ramsay Hunt's syndrome? How to treat?**A:** It is the herpes zoster of geniculate ganglia characterized by:

- Ipsilateral VIIth cranial nerve palsy (lower motor neuron).
- Rash (herpetic vesicles) in the external auditory meatus and soft palate.
- Ipsilateral loss of taste and buccal ulceration.
- Deafness and Vth nerve lesion may also occur.

Treatment: Antiviral (famciclovir) may be given. However, complete recovery is less likely than Bell's palsy.

Q: What are the causes of bilateral facial palsy and bilateral facial weakness?**A:** As follows:**Causes of bilateral facial palsy:**

- Guillain–Barré syndrome (GBS).
- Sarcoidosis.
- Bilateral Bell palsy (rare).
- Bilateral parotid disease.
- Lyme disease.
- Any cause of mononeuritis multiplex (rare).

Causes of bilateral facial weakness:

- Bilateral facial palsy.
- Myasthenia gravis.
- Myopathy (facio–scapulo–humeral myopathy and myotonic dystrophy).

N.B.: Myasthenia gravis and some myopathy may mimic bilateral facial palsy. However, these are not due to nerve involvement.

Presentation of a Case (LMN Type of Facial Palsy): Case No. 3

- Just like Case 1, but there is no Bell's phenomenon.

My diagnosis is **LMN type of facial palsy**.

Q: Why LMN type of facial palsy?

A: Because both upper and lower parts of face are affected.

Q: Why not UMN type of facial palsy?

A: In UMN of facial palsy, only lower part of face is involved, as muscles of upper part of face are bilaterally innervated.

Q: How to locate the site of lesion in LMN facial palsy and what are the causes?

A: As follows:

1. Lesion in pons:
 - Associated VIth nerve palsy (lateral rectus muscle of eye) and Vth nerve palsy.
 - If corticospinal tract is involved, there is contralateral hemiplegia (Causes are: vascular, demyelinating disease, tumour, syringobulbia).
2. Cerebellopontine angle lesion:
 - Usually associated with Vth, VIth, VIIth and VIIIth nerve palsy and also cerebellar signs (Causes are: acoustic neuroma, neurofibroma, meningioma).
3. Lesion in petrous part of temporal bone:
 - Associated with loss of taste in anterior 2/3rd of tongue and also hyperacusis (Causes are: Bell's palsy, Ramsay Hunt's syndrome, trauma, chronic suppurative otitis media).
4. Lesion in face:
 - Parotid disease such as: Parotid tumour, sarcoidosis, trauma or surgery of parotid gland.

Presentation of a Case (UMN Type—Supposing on Right Side): Case No. 4

- Asymmetry of face on the right side. Wrinkling of forehead is normal on both sides.
- The patient can close the eyes properly (upper part of face is not involved).
- There is involvement of lower part of face (as evidenced by impaired puffing of cheek, smiling, whistling and showing teeth).

My diagnosis is **Right sided UMN type of facial palsy**.

Q: Why UMN lesion? What else do you want to see and Why?

A: It is UMN lesion because only the lower part of face is affected and upper part is spared. I want to see if the patient has hemiplegia (ask the patient to raise the arms and legs), because common cause of UMN facial palsy is CVD involving internal capsule, which is associated with hemiplegia.

Q: Is there any **isolated UMN facial palsy** without hemiplegia?

A: Yes, if the lesion occurs in the contralateral frontal complex (involving inferior frontal branch of middle cerebral artery).

Q: What are the **differences** between UMN and LMN type of facial palsy?

A: As follows:

Topic	UMN	LMN
1. Site of lesion	Above the facial nucleus, commonly in internal capsule	In the facial nucleus and distal to the nucleus
2. Involved area	Lower part of face	Both upper and lower part of face
3. Bell's phenomenon	Absent	May be present
4. Taste sensation	Not affected	May be affected
5. Hyperacusis	Absent	May occur, if nerve to the stapedius is involved
6. Facial wasting or atrophy	Absent	May be present
7. Associated feature	Usually associated with hemiplegia	Not so (contralateral hemiplegia, if pontine lesion); other findings according to site of lesion

VITH NERVE PALSY

Instruction by the examiner:

- Examine the eyes or look at the eyes. What else do you want to examine?
- See the movement of eyes.

Presentation of a Case (Supposing Right Sided):

- The patient has convergence squint in right eye at rest.
- No lateral movement of right eye.
- On attempting to look on that side, there is diplopia (outermost image comes from the affected eye).
- The outer image disappears on covering the affected eye.
- Other movements of the eye are normal.
- Pupil: Normal.

My diagnosis is **Right sided VIth nerve palsy**.

Q: What does **diplopia** look like in VIth nerve palsy?

A: Image looks parallel and horizontal to each other (if the image is oblique or angular, it indicates superior oblique palsy).

Q: What are the **causes of VIth nerve palsy**?

A: As follows:

- Raised intracranial pressure (common cause), due to stretching of the nerve in its long intracranial course (a false localizing sign).
- Brainstem lesion (vascular, neoplastic, multiple sclerosis).
- Cavernous sinus lesion (tumour, thrombosis, infection, aneurysm).
- Trauma.
- Any cause of mononeuritis multiplex.
- Idiopathic (common).
- Subacute meningitis (due to fungal, tuberculous, lymphomatous, carcinomatous).
- Diabetes mellitus.
- Others: Sarcoidosis, giant cell arteritis, Lyme disease, acoustic neuroma, nasopharyngeal carcinoma.



Right-sided VIth nerve palsy



Right-sided VIth nerve palsy—failure of abduction

Q: What are the **causes of bilateral VIth nerve palsy**?

A: As follows:

- Trauma.
- Wernicke's encephalopathy.
- Mononeuritis multiplex.
- Raised intracranial pressure (VIth nerve palsy is often associated with VIIth nerve lesion also).

MULTIPLE CRANIAL NERVE PALSY

Instruction by the examiner:

- Examine the eyes or look at the eyes. What else do you want to examine?
- See the movement of eyes.

Presentation of a Case (Supposing IIIrd, IVth and VIth Nerve Palsy): Case No. 1

- There is ptosis.
- No movement of eyeball in any direction.
- On attempting to look at the right or left, there is diplopia.
- Pupil is dilated, no reaction to light, both direct and consensual.

My diagnosis is **IIIrd, IVth and VIth nerve palsy**.

Q: What are the causes?

A: As follows:

1. Raised intracranial pressure due to any cause:
 - Meningitis.
 - Encephalitis.
 - Sarcoidosis.
 - Neoplasm.
 - GBS.
2. Brainstem lesion:
 - Vascular (CVD).
 - Neurosyphilis.
 - Multiple Sclerosis.
 - Syringobulbia.
3. Mononeuritis multiplex (due to any cause).
4. Cavernous sinus thrombosis or carotid-cavernous fistula.

Presentation of a Case (IIIrd and VIth Nerve Lesion—Supposing Right Side): Case No. 2

- There is ptosis on right side.
- Pupil is dilated, no reaction to light (both direct and consensual).
- There is failure of lateral movement of eye, also there is failure of upward and downward (eye on abduction) and upward movement (eye on adduction) and medial movement.
- Diplopia is present on movement of the lateral gaze.

My diagnosis is **Right-sided IIIrd and VIth cranial nerve lesion**.



Left-sided ptosis due to IIIrd nerve palsy



Left eye—failure of adduction and dilated pupil (IIIrd nerve palsy)



Left-sided ptosis and failure of wrinkling due to facial palsy



Failure of abduction (left) due to VIth nerve palsy

Q: What are the causes?

A: As follows:

- Raised intracranial pressure due to any cause.
- Mononeuritis multiplex.
- Meningitis.
- Encephalitis.
- Trauma.



Failure of elevation and depression of eyeball (inferior and superior oblique palsy—eyeball medially)



Failure of elevation and depression of eyeball (superior and inferior rectus palsy—eyeball laterally)



Left IIIrd nerve palsy and right VIIth nerve palsy

Presentation of a Case (IXth, Xth and XIIth Cranial Nerve Palsy): Case No. 3

- There is hoarseness of voice, nasal regurgitation and nasal voice.
- Palate movement is absent.
- Gag reflex is absent.
- Tongue is spastic, wasted and weak. There is fasciculation in the tongue.

My diagnosis is **IXth, Xth and XIIth cranial nerve palsy.**

Q: What are the **causes** of IX, X, XI and XIIth cranial nerve palsy?

A: According to the site of lesion:

1. Within the brainstem:
 - Infarction.
 - Syringobulbia.
 - MND.
 - Poliomyelitis.
2. At the skull base:
 - Carcinoma of nasopharynx.
 - Glomus tumour.
 - Neurofibroma.
 - Jugular venous thrombosis.
 - Trauma.
3. Within the neck and nasopharynx:
 - Carcinoma of nasopharynx.
 - Metastases.
 - Carotid artery dissection (XII).
 - Polyneuropathy.
 - Trauma.
 - Lymph node biopsy in posterior triangle (XI).
4. Others:
 - GBS.
 - Tubercular meningitis.
 - Carcinomatous meningitis.
 - Encephalitis.
 - Brainstem lesion: vascular (CVD) and neoplastic.
 - Bulbar and pseudobulbar palsy.
 - Neurosyphilis.
 - Mononeuritis multiplex.

Remember the site of lesion involving multiple cranial nerves:

- Unilateral IIIrd, IVth, Vth and VIth nerve involvement suggests lesion in cavernous sinus.
- Unilateral Vth, VIIth and VIIIth nerve involvement suggests lesion in cerebellopontine angle.
- Unilateral IXth, Xth and XIth nerve involvement suggests lesion in jugular foramen.
- Combined bilateral Xth, XIth and XIIth nerve involvement suggests bulbar palsy, if LMN lesion signs are present; and pseudobulbar palsy, if UMN lesion signs are present.

Actions of extraocular muscles:

- When eye is abducted, elevator is superior rectus and depressor is inferior rectus (both supplied by IIIrd nerve).
- When eye is adducted, elevator is inferior oblique (supplied by IIIrd nerve) and depressor is superior oblique (supplied by IVth nerve).

CVD WITH HEMIPLEGIA

Instruction by the examiner:

- Examine the lower limbs, **Or** examine the upper limbs.
- Perform the neurological examination of upper or lower limbs.

Presentation of a Case:

- There is difficulty in raising the right leg and right arm.
- Muscle tone is increased in both right upper and lower limbs, but normal in left limbs.
- Motor power is diminished, grade 0/5 in right upper and lower limbs, but normal in left side.
- Deep tendon reflexes are exaggerated in right limbs and normal in left limbs.
- There is ankle clonus on the right side.
- Plantar response is extensor on the right side and flexor on the left side.
- Sensory functions: normal.
- There is a urinary catheter in situ.

My diagnosis is **Right-sided hemiplegia more likely with CVD.**

Q: What **else** do you want to examine?

A: I want to examine speech and cranial nerves. Also, blood pressure, heart and neck (bruit) to find out the cause.

Q: What would you look for in the **heart**?

A: Any arrhythmia like atrial fibrillation and any valvular lesion (may cause cerebral embolism).

Q: What would you look for in the **neck**?

A: Carotid bruit (thrombus from carotid may be dislodged and cause cerebral thrombosis).

Q: What is the **cause** of CVD in this patient?

A: I would like to take the history of hypertension, any cardiac problem and also the onset, history of unconsciousness, headache etc. Causes may be:

- Cerebral infarction: Commonest cause.
- Cerebral haemorrhage.

Q: What is the likely **site of lesion** in your case?

A: Left internal capsule due to involvement of lenticulostriate branch of middle cerebral artery.

Q: What are the **diseases** included in **CVD**?

A: As follows:

- Cerebral haemorrhage.
- Cerebral thrombosis (causing cerebral infarction).
- Cerebral embolism (causing cerebral infarction).
- Subarachnoid haemorrhage.
- Hypertensive encephalopathy.
- Cerebellar haemorrhage.
- Cerebellar infarction.

Q: What investigations do you suggest?**A:** As follows:

1. CT scan of head (first investigation to be done).
2. Complete blood count with ESR.
3. Blood sugar.
4. Blood urea and serum creatinine.
5. Fasting lipid profile.
6. Serum electrolytes.
7. Chest X-ray PA view.
8. ECG.
9. To find out the source:
 - Doppler study of extra-/intracranial vessels.
 - Echocardiography (transthoracic or transoesophageal).
 - MRA or CTA of the cerebral vessels.
 - DSA of cerebral vessels (gold standard to find out AVM or aneurysm).

Q: What is stroke? What are the types of stroke?**A:** Stroke may be defined as sudden development of focal neurological deficit due to non-traumatic vascular cause, lasting for more than 24 hours. It is of following subvarieties:

- Transient ischaemic attack (TIA): Sudden neurological dysfunction due to cerebral ischaemia lasting less than 24 hours and the patient recovers completely within 24 hours.
- Stroke in evolution: The symptoms worsen gradually or in a step-wise pattern over hours or days, the neurological deficit persists for more than 24 hours.
- Completed stroke: Clinical signs of neurological deficit are persistent.
- Reversible ischaemic neurological deficit (RIND): Neurological deficit persists for more than 24 hours, but recovers completely within 3 weeks.
- Partial non-progressive stroke (PNS): Neurological deficit persists for more than 3 weeks, but is either partial or ends up with minimal residual deficit.

Q: What are the features of CVD according to the site of involvement of different parts of brain?**A:** As follows:

1. Cortical:
 - Usually monoplegia.
 - If lesion is extensive, contralateral hemiplegia may occur.
 - Speech disturbance may be present, if the lesion involves the dominant hemisphere.
 - Jacksonian convulsions and headache may occur.
 - There may be cortical type of sensory loss, e.g., astereognosis.
2. Subcortical:
 - Usually monoplegia.
 - May be contralateral hemiplegia.
 - Speech disturbance may be present.
 - There may be loss of postural sensibility, tactile localization and discrimination of affected limbs due to involvement of thalamo-cortical fibres.

3. Internal capsule:

- Contralateral hemiplegia.
- Hemianaesthesia due to damage of sensory fibres and homonymous hemianopia due to damage of visual fibres, both of which lie posterior to the pyramidal tract in internal capsule.
- Global aphasia in left sided lesion.
- VIIth cranial nerve palsy on the side of palsy (UMN type).

4. Brainstem:

- Symptoms: Vertigo, nausea, vomiting.
- Crossed hemiplegia, brainstem syndrome, pupillary abnormality, cerebellar involvement, gaze paralysis, Horner's syndrome.
- If pons is involved: There is deep coma, pin point pupil (PPP), hyperpyrexia, decerebrate or decortical rigidity, absence of lateral eye movement on head turning.
- If mid brain and medulla are involvement: There is loss of consciousness, quadriplegia, Cheyne–Stokes breathing, decerebrate rigidity.

Q: How to treat CVD?**A:** As follows:

1. General measures:

- Nasogastric tube feeding.
- Regular change of posture (2 hourly).
- Care of bowel, bladder (catheterization), mouth (to prevent fungal infection), eyes (tear naturale or taping of the affected eye to shut).

2. Control of risk factors: Hypertension, diabetes mellitus, hyperlipidaemia etc.

3. If cerebral oedema: Dexamethasone or mannitol.

4. Specific treatment according to the type of stroke (after CT scan):

- Cerebral infarction: Antiplatelet drugs (e.g., aspirin, clopidogrel). Cerebral vasodilator like vinpocetin should be given. If atrial fibrillation, heparin followed by warfarin should be considered.
- Cerebral haemorrhage: For massive haemorrhage, neurosurgical intervention may be required. Other treatment is symptomatic and supportive.
- Subarachnoid haemorrhage: Nimodipine can be given, neurosurgical intervention is essential.

5. To reduce morbidity and improve quality of life: Physiotherapy, speech therapy, occupational therapy etc.

Q: What is the prognosis of CVD?**A:** Prognosis depends on type of lesion, site, extent of involvement and associated primary risk factors.

1. Mortality rate is higher in intracerebral haemorrhage than embolic stroke.
2. In cerebral infarction, immediate prognosis is better, long-term prognosis depends upon extent of damage.
3. In cerebral haemorrhage, immediate prognosis is worse.
 - In haemorrhagic stroke: 25% die within first 2 years, 10% die within first month. However, prognosis is better in the long run, when the haematoma resolves.
 - One-third returns to independent mobility, one-third becomes disabled.

Q: What are the causes of recurrent hemiplegia?**A:** As follows:

1. CVD due to:
 - Atrial fibrillation.
 - Hyperviscosity syndrome.
 - Homocystinuria.
 - Amyloidosis.
 - Deficiency of protein C, S or antithrombin III.
 - Polycythaemia rubra vera.
 - Antiphospholipid syndrome.
 - Polyarteritis nodosa.
 - Wegener's granulomatosis.
 - Takayasu's arteritis.
2. Other causes:
 - Multiple Sclerosis.
 - Hemiplegic migraine.
 - Epilepsy (Todd's palsy).
 - Hysterical hemiplegia.

Q: What are the causes of CVD in a young patient?**A:** As follows:

- Mitral stenosis with atrial fibrillation (may cause cerebral embolism from cardiac source).
- Other cardiac cause: PFO, VSD, TOF.
- Antiphospholipid syndrome.
- SLE.
- Haematological disease: Sick cell anaemia, polycythaemia rubra vera, inherited deficiency of naturally occurring anticoagulant (protein C, protein S, antithrombin III, factor V Leiden). In all these conditions, there is increased tendency to thrombosis.
- Vasculitis, Behcet's disease.
- Vascular malformation: AVM, berry aneurysm causing SAH.
- Dissecting aneurysm.
- In female: Oral contraceptive pill, eclampsia.
- Homocystinuria.
- Syphilis.
- Premature atherosclerosis may occur in familial hyperlipidaemia.
- Rarely, migraine may cause cerebral infarction.
- Drugs like amphetamine, cocaine.

Q: What investigations should be done in a young patient with stroke?**A:** According to the cause:

- CBC, ESR: It will also exclude polycythaemia rubra vera.
- Chest X-ray, ECG and echocardiography (to exclude cardiac problem like mitral stenosis with atrial fibrillation, other cardiac problem like PFO, TOF).
- Serum lipid profile: To exclude juvenile hyperlipidaemia.
- For collagen vascular disease: ANA, anti-dsDNA, anticardiolipin and antiphospholipid antibody.
- P-ANCA, C-ANCA.
- Coagulation screening, serum antithrombin III, protein C and protein S level.
- Others: Red cell mass (in PRV), chromatographic test in serum and urinary level of homocystine or methionine (in homocystinuria), TPHA and VDRL (in syphilis).

Q: What are the **risk factors** for stroke?

A: Risk factors are variable for ischaemic stroke and haemorrhagic stroke:

Risk factors for **ischaemic** stroke:

1. Non-modifiable:

- Age.
- Gender.
- Ethnicity or race.
- Genetics.
- Family history.

2. Modifiable:

- Lifestyle.
- Smoking.
- Obesity.
- Hypertension.
- Diabetes mellitus.
- Heart disease (atrial fibrillation, ischaemic heart disease, cardiomyopathy etc.).
- Dyslipidaemia.
- Oral contraceptive pill.
- Alcohol.
- Previous history of stroke or TIA.
- Carotid vessel atherosclerosis.
- Atheromatous aortic arch.
- Anti-phospholipid syndrome.
- Deficiency of protein C, S and antithrombin III.
- Vasculitis (like polyarteritis nodosa, Wegener's granulomatosis, Takayasu's arteritis), migraine.
- Others: homocystinuria, hyperfibrinogenaemia, polycythaemia rubra vera, thrombotic thrombocytopenic purpura, sickle cell anaemia, protein V Leiden syndrome.
- Abuse of cocaine, use of COX-2 inhibitor (slightly increased incidence of stroke).

Risk factors for **haemorrhagic** stroke:

- Hypertension.
- AVM.
- Aneurysm.
- Amyloid angiopathy.
- Cavernous angioma.
- Anticoagulant therapy.
- Hypercoagulable disorder.
- Drugs: Cocaine, amphetamine.
- Vasculitis: SLE, polyarteritis nodosa, isolated CNS vasculitis.
- Septicaemia.
- Moyamoya disease.
- Haemorrhage into brain tumour.

Q: How to prevent stroke?**A:** As follows:

- Risk factors like hypertension, diabetes mellitus, obesity etc. should be identified and controlled.
- Smoking and alcohol should be stopped.
- Regular physical exercise.
- Avoid stress, anxiety, tension.
- Antiplatelet drug, e.g., aspirin, clopidogrel.
- Life style modification: Regular physical exercise, dietary modification.
- Statin should be given to all patients.
- If there is atrial fibrillation: Treatment of primary cause and anticoagulation.
- Treatment of primary cause.

Brainstem syndrome:

1. Weber's syndrome: Ipsilateral paralysis of IIIrd cranial nerve (LMN type) with contralateral hemiplegia (crossed hemiplegia). Paralysis of upward gaze is usually present. **Lesion is at midbrain.**
2. Millard–Gubler's syndrome: Paralysis of VIth cranial nerve (LMN type) with or without VIIth cranial nerve palsy (LMN type) with contralateral hemiplegia (crossed hemiplegia). **Lesion is at pons.**
3. Lateral medullary syndrome (posterior inferior cerebellar artery thrombosis, also called Wallenberg syndrome): The patient presents with acute vertigo, nausea, vomiting and diplopia, cerebellar and other signs. Features depend on the precise structures damaged such as:
 - a) Ipsilateral:
 - Trigeminal nerve lesion: Diminished pain and temperature (due to involvement of descending tract and nucleus of trigeminal nerve).
 - Cerebellar signs (due to involvement of cerebellum and its connection).
 - Horner's syndrome (due to involvement of descending sympathetic tract).
 - Palatal paralysis and diminished gag reflex (there may be hoarseness and dysphagia due to vocal cord paralysis because of IXth and Xth cranial nerve lesion).
 - Diplopia (due to VIth nerve involvement).
 - b) Contralateral:
 - Loss of pain and temperature (in the trunk, limbs, may be in face) due to spinothalamic tract involvement. It is called dissociated sensory loss.
 - c) When isolated occlusion of PICA, pyramidal pathways escape and there is no hemiplegia. However, in the majority of cases, there is vertebral artery involvement and pyramidal signs (hemiplegia) are present.
4. Medial medullary syndrome:
 - It is due to occlusion of lower basilar artery or vertebral artery or one of its medial branches. It is characterized by contralateral hemiplegia, which spares the face, contralateral loss of vibration and joint position sense, ipsilateral paralysis and wasting of tongue.

N.B.: Remember the following points:

- Damage to brainstem reticular activating system leads to coma.
- Upper brainstem infarction (ventral pons) leads to locked in syndrome.
- Pseudobulbar palsy may occur after lower brainstem infarction (medullary infarction, bilateral cerebral infarction).

Q: What are the **causes of coma** or unconsciousness?

A: As follows (remember the mnemonic **AEIOU–DAMH**):

- **A**poplexy: Cerebral haemorrhage, subarachnoid haemorrhage etc.
- **E**pilepsy.
- **I**nfection (e.g., encephalitis, meningitis, cerebral malaria, severe septicaemia).
- **O**pium poisoning.
- **U**raemia (renal failure).
- **D**iabetes mellitus (ketoacidosis, hypoglycaemia, lactic acidosis, hyperosmolar nonketotic diabetic coma or hyperglycaemic hyperosmolar state).
- **D**rug poisoning such as sedative.
- **A**lcohol.
- **M**etabolic: Metabolic acidosis.
- **H**ypoglycaemia, hypoxaemia, hypertensive encephalopathy, hepatic coma, hypothyroidism (myxoedema coma), hyponatraemia, hypothermia, hyperpyrexia, head injury.

GAIT ABNORMALITY

Instruction by the examiner:

- Look at the gait. What is your diagnosis?

Presentation of a Case:

- The patient has broad-based reeling or drunken gait.

My diagnosis is **Cerebellar gait**.

Q: What else do you like to see?

A: I would like to see other signs of cerebellar lesion, such as:

- Titubation.
- Tilting towards the site of lesion.
- Nystagmus (horizontal).
- Scanning speech.
- Intention tremor.
- Incoordination.
- Dysdiadochokinesis.
- Past-pointing (dysmetria).
- Ataxia.
- Hypotonia.
- Diminished tendon reflex (knee jerk may be pendular).

Q: What are the causes of cerebellar lesion?

A: See in 'cerebellar lesion'.

Q: What are different types of gait?

A: As follows:

- Cerebellar gait (Ataxic gait): Broad-based reeling or drunken gait. It is found in cerebellar lesion.
- Parkinsonian gait: Festinate gait (for details, see in 'Parkinsonism').
- Stomping gait (Sensory gait): The patient raises the foot suddenly and tends to throw forward, bringing it to the ground with a stomp, often heel first. Found in sensory ataxia.
- **High stepping gait** (neuropathic or equine gait): The patient lifts his foot high to avoid scrapping the toes. Found in foot drop.
- Hemiplegic gait: The patient has difficulty in bending the knee and drags the hemiplegic limb in a semicircle-like motion with the toes scrapping the floor and forefoot flops to the ground before the heel. Found in hemiplegia.
- Scissor gait (Diplegic): During walking, one leg crosses in front of other. Found in spastic paraplegia, cerebral palsy.
- **Waddling gait (Myopathic gait)**: The patient walks on a wide base with trunk moving side to side and pelvis drooping on each side. At each step, toes touch the ground before heel. Found in myopathy, osteodystrophy, bilateral hip joint disease. There is lumbar lordosis.

- Marche a petit pas (Apraxic gait): There is slow movement. The patient walks with very short, shuffling and irregular steps with loss of associated movements. It is similar to that of Parkinson's disease (except, there is no resting tremor, retained arm swinging, upright posture and wide based stance). Found in normal pressure hydrocephalus.
- Choreiform gait (Hyperkinetic gait): Irregular, jerky, dance like, involuntary movement in all extremities. Found in Sydenham's chorea, Huntington's disease and other forms of chorea, athetosis or dystonia.

Q: What is astasia abasia?

A: Astasia means inability to stand upright without assistance. Abasia means the base of gait is inconstant or unmeasurable. Found in patient with psychogenic disturbance. The patient is unable to walk, to stand, falls far to the side on walking but usually regains balance before hitting the ground. The legs may be thrown out widely or the patient may kneel with each step.

Q: What is antalgic gait?

A: It is a type of gait adopted to avoid pain on weight bearing structures, characterized by very short steps with fixed leg posture. It is due to painful condition of joints (such as hip, knee, ankle) or injury to the bones or soft tissue.

OROFACIAL DYSKINESIA

Instruction by the examiner:

- Look at the face. Or look at the patient.

Presentation of a Case:

- There is orofacial dyskinesia with chewing, pouting, lip smacking, grimacing, tongue movement associated with choreo-athetosis of the limbs and trunk.

My diagnosis is **Orofacial dyskinesia**.

Q: What **history** do you like to take?

A: I would like to take drug history. Usually, there is history of prolonged intake of neuroleptic drugs.

Q: If there is history taking **neuroleptic** drugs, what will be the diagnosis?

A: Tardive dyskinesia. Tardive means after chronic exposure to dopamine receptor blockers (such as antipsychotic, antiemetic).

Q: What is **tardive dyskinesia**?

A: Tardive dyskinesia (TD) is a drug induced disorder characterized by orofacial dyskinesia such as lip smacking, chewing, pouting, grimacing, rhythmic tongue movement and choreo-athetoid movement.

Involuntary movements involve the tongue, lips, face, trunk and extremities that have persisted for at least 4 weeks and that began during treatment with neuroleptics or within 4 weeks of discontinuing neuroleptics.

To diagnose TD, there is history of neuroleptics for at least 3 months. It may persist or even worse after withdrawal of drug.

TD is common in schizophrenia, schizo-affective disorder or bipolar disorder who are treated with antipsychotic drugs for long period, but occasionally occur in other patients as well.

TD is due to altered dopamine receptor sensitivity induced by the drug.

Q: What drugs may **cause** tardive dyskinesia?

A: Usually neuroleptics: phenothiazines (e.g., chlorpromazine), butyrophenones (e.g., haloperidol). Other drugs:

- Antiemetic: Metoclopramide (D₂ dopamine receptor antagonist).
- Antiepileptic: Phenytoin, carbamazepine, phenobarbital, ethosuximide.
- Others: Tetrabenazine, antihistamines, fluoxetine, amoxapine.

N.B.: *Quetiapine and olanzapine causes less TD.*

Q: What **other extrapyramidal complications** due to neuroleptics?

A: As follows:

- Acute dystonia: Occurs soon after starting the drug. Usually due to metoclopramide, prochlorperazine (it is treated by IV benztropine or procyclidine. Offending drug should be stopped).
- Akathisia (uncontrollable restlessness, repetitive and irresistible need to move).
- Parkinsonism.

Q: How to **treat TD**?

A: The drug should be stopped. Tetrabenazine may help.

Q: What are the **different types** of dyskinesias?

A: As follows:

- Chorea.
- Athetosis.
- Tic.
- Tortion dystonia.
- Hemiballismus.

FOOT DROP (COMMON PERONEAL NERVE PALSY)

Instruction by the examiner:

- Examine the lower limb of the patient.

Presentation of a Case (Supposing Right Side):

- There is wasting of anterior tibial and peroneal group of muscles on the right lower limb.
- Dorsiflexion and eversion of right foot is weak (ankle inversion is spared).
- There is dorsiflexion of 1st toe.
- Ankle jerk is normal.
- Sensation over the lateral aspect of right leg and dorsum of right foot is impaired.

My diagnosis is **Right-sided foot drop** (comment on caliper shoes or splint, if any).

N.B.: look for thickening of common peroneal nerve and also hypopigmented anaesthetic patch on the right leg. If present, indicates leprosy.



Foot drop (right)



Foot drop (left)



Unable to dorsiflex (right sided foot drop)

Q: Where is the **lesion**?

A: Common peroneal nerve (lateral popliteal nerve, L_{4,5}) palsy.

Q: What are the **branches** of common peroneal nerve?

A: 2 branches:

- Superficial peroneal nerve: Sensory to lateral calf and dorsum of foot, also responsible for eversion of foot (motor).
- Deep peroneal nerve: Dorsiflexion of foot and toe, sensation to the web space between 1st and 2nd toes.

Q: Can it be due to deep peroneal nerve palsy?

A: In deep peroneal nerve palsy, the sensory deficit will be limited to the area between 1st and 2nd toes.

Q: What are the **reflex and planter responses** in common peroneal nerve palsy?

A: Both normal.

Q: What **else** do you like to examine? What **findings** do you expect?

A: I want to examine the gait, which is high stepping gait (the patient lifts his foot high to avoid dragging the forefoot and there is an audible 'clap' of the foot as he walks). Also, the patient will be unable to stand on the affected heel.

Q: What is the **site** of the lesion of common peroneal nerve palsy?

A: The nerve is usually injured at the head of the fibula due to fracture or compression by a tourniquet or splint.

Q: What are the **causes** of common peroneal nerve palsy?

A: As follows:

- Trauma (to the nerve, fibular fracture, total knee arthroplasty or proximal tibial osteotomy).
- Compression by plaster of Parris cast or tourniquet around the knee.
- Compression by ganglion arising from superior tibio-fibular joint.
- Leprosy.
- Old polio.
- Any cause of mononeuritis multiplex (diabetes mellitus, polyarteritis nodosa, collagen vascular disease).

Q: What is the **commonest cause**?

A: Leprosy.

Q: What **investigation** should be done to diagnose common peroneal nerve palsy?

A: Nerve conduction study (shows local conduction block or slowing in the region of head of fibula).

Q: How to **treat** common peroneal nerve palsy?

A: As follows:

- Surgery, if the nerve is severed.
- Use of splint and calliper shoes for intact and concussed nerve.
- Treatment of primary cause, if any.

Q: What are the **causes** of foot drop?

A: As follows:

- Peripheral neuropathy.
- Common peroneal nerve palsy.
- Sciatic nerve palsy.
- Motor neuron disease.
- L₄, L₅ root lesion.
- L₄, L₅ disc prolapse.
- Lumbosacral plexus lesion.
- Chronic lead or arsenic poisoning.
- Myotonic dystrophy.
- Charcot–Marie–Tooth disease.

Q: What are the **causes**, if a patient is unable to walk on heel?

A: As follows:

- Common peroneal nerve palsy
- Charcot–Marie–Tooth disease

CHARCOT–MARIE–TOOTH DISEASE (PERONEAL MUSCLE ATROPHY)

Instruction by the examiner:

- Examine the lower limbs of this patient. Or perform the neurological examination of lower limbs.

Presentation of a Case: Case No. 1 (Lower Limbs)—

- Bilateral pes cavus and clawing of toes are present.
- There is wasting of distal muscles of both lower limbs up to the middle of legs, giving rise to inverted champagne bottle appearance (stork or spindle legs).
- Fasciculation (may be present).
- Dorsiflexion: Weak in both feet.
- Ankle jerk: Absent bilaterally.
- Plantar response: equivocal or absent on both sides.
- Sensory: Mild impairment of both superficial and deep sensation up to middle of legs (sometimes marked sensory loss with trophic ulcer may be found).
- Gait: High steppage gait with foot drop.
- Rombergism may be positive.

My diagnosis is **Distal motor and sensory neuropathy**, most likely **Charcot–Marie–Tooth disease**.

N.B.: Always look for scar in the neck of the fibula. If present, it is suggestive of trauma or fracture that may cause common peroneal nerve lesion. Palpate the nerve that may be thickened (important feature in CMT).



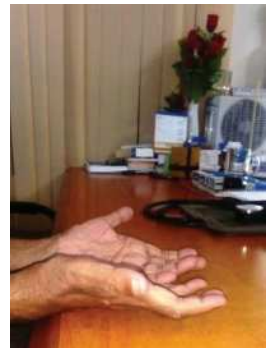
Inverted-champagne-bottle appearance



Pes cavus



Pes cavus with clawing of toes



Claw hand with wasting of small muscles of hand

Q: What else do you want to see?

A: I want to examine the upper limbs. There may be wasting of small muscles of hands and arm muscles with claw hand.

Presentation of a Case: Case No. 1 (Upper Limbs):

- There is claw hand and wasting of distal muscles of both upper limbs up to the middle of forearm.
- Weakness of small muscles of hand.
- Reflex: Absent.
- Sensory function is reduced distally in gloves distribution.

My diagnosis is **Distal motor and sensory neuropathy**, most likely **Charcot–Marie–Tooth disease**.

Q: What else do you want to see?

A: I want to examine the lower limbs. There may be pes cavus, inverted champagne bottle appearance.

Q: How does the patient present?

A: The patient usually presents with foot deformities or gait disturbance in early childhood or early adult life. Slow progression leads to features of polyneuropathy with distal weakness and wasting that begins in leg, associated with distal sensory loss. There is depressed or absent tendon reflexes.

N.B.: Usually, lower limbs are affected earlier than upper limbs.

Q: What is the mode of inheritance?

A: Variable, may be autosomal dominant or recessive or X-linked. Affected family members may have forme fruste with only pes cavus and absent ankle jerks.

Q: What are the types of peroneal muscular atrophy?

A: As follows:

- Hereditary motor and sensory neuropathy type-I: There is demyelinating neuropathy. It is the commonest type (70%), inherited as autosomal dominant. NCV is reduced.
- Hereditary motor and sensory neuropathy type-II: There is axonal neuropathy with prominent sensory involvement, pain and paraesthesia. It is inherited as autosomal dominant and autosomal recessive. NCV is relatively normal.
- Hereditary motor and sensory neuropathy type-III (also called Dejerine–Sottas disease): There is demyelinating neuropathy. NCV is reduced.
- Other types: CMT with optic atrophy, deafness, retinitis pigmentosa and spastic paraparesis.
- Rarely another type: CMTX, an X-linked dominant hereditary motor sensory neuropathy (HMSN).

Q: What investigation do you suggest?

A: Nerve conduction velocity.

- In HMSN type-I: There is marked reduction in motor and sensory conduction velocity.
- In HMSN type-II: Motor conduction velocity is normal or slightly reduced, sensory nerve action potential may be absent and signs of chronic partial denervation are found in affected muscles electromyography.

Q: How to treat?

A: No curative treatment, only symptomatic.

- Reassurance and education to the patient.
- Regular exercise and physiotherapy.
- Walking aids.
- Occupational therapy.
- Orthopaedic measures for correction.

Q: What is the prognosis of this disease?

A: It is slowly progressive, arrests in middle life. Lifespan is usually normal. Abortive cases are common. Degree of disability is less in spite of marked deformity.

Q: What are the causes of pes cavus?

A: It may be unilateral or bilateral.

1. Cause of bilateral pes cavus:

- Charcot–Marie–Tooth disease.
- Friedreich's ataxia.
- Muscular dystrophies.
- Spinal muscular atrophy.
- Cerebral palsy.
- Syringomyelia.
- Hereditary spastic paraparesis.
- Spinal cord tumour.

2. Cause of unilateral pes cavus:

- Old poliomyelitis.
- Spinal trauma.
- Spinal cord tumour.
- Mal-union of calcaneus or talus fracture.

Q: What is the mechanism of pes cavus in Charcot–Marie–Tooth disease?

A: There is weakness of anterior tibialis and peroneus muscles. Posterior tibialis and peroneus longus antagonize these muscles resulting in pes cavus.

CERVICAL MYELOPATHY

Instruction by the examiner:

- Examine the lower limbs or perform the neurological examination of the lower limbs. Or,
- Examine the upper limbs or perform the neurological examination of the upper limbs.

Presentation of a Case: Case No. 1 (Upper Limbs):

- There are few fasciculations in the forearm.
- Also, there is generalized wasting of small muscles of hands involving the thenar, hypothenar and interossei muscles.
- Weakness of small muscles of hand.
- Muscle tone and power are reduced.
- Reflex: Loss of biceps and supinator jerks but triceps is exaggerated (inversion of reflex).
- Sensory function is reduced or absent in C_{5,6} distribution.
- When the eyes are closed and the hands are outstretched and supinated, there is abduction of little finger (called myelopathy hand sign, there is deficient or failure of adduction or extension of ulnar 2 fingers). There is also unconscious writhing of fingers (pseudoathetosis).
- Loss of vibration and position sense (dorsal column sign).

My diagnosis is **Cervical myelopathy**.

N.B.: Inversion of reflex means loss of biceps or brachioradialis but exaggerated triceps response (lesion in C₅ or C₆).

Q: What other signs can be seen in hand in cervical myelopathy?

A: As follows:

1. **Grip and release test:** normally a patient can make a fist and release 20 times in 10 seconds. Myelopathic patients may struggle to do this.
2. **Dynamic Hoffman's sign:** snapping patients distal phalanx of middle finger leads to spontaneous flexion of other fingers (Hoffman's sign). If the sign is negative, it can be tested by flexion and extension of the neck, may become positive during the manoeuvre, which indicates cervical spondylotic myelopathy (Dynamic Hoffman's sign).

Q: What else do you want to examine?

A: I want to examine the lower limbs. There may be features of UMN lesion with dorsal column lesion signs in lower limbs.

Presentation of a Case: Case No. 2 (Lower Limbs):

- Both flexor and extensor muscles are weak (mention the grade) with hypertonia in both lower limbs (may be clasp knife, mention if any).
- Knee and ankle jerks are exaggerated with extensor plantar response on both sides.
- There is ankle clonus in right or left or both (mention, if any).
- Co-ordination is impaired in right or left or both (mention, if any).
- Sensory abnormalities are absent.
- Vibration and position senses are lost (dorsal column sign).
- Gait disturbance with positive Robergism.

My diagnosis is **Spastic paraplegia with dorsal column sign**. My differential diagnosis are:

- Cervical myelopathy.
- Friedrich's ataxia.
- Multiple sclerosis.
- Taboparesis.
- Subacute combined degeneration of spinal cord.

N.B.: Remember the following points:

- *Typical finding in cervical myelopathy is LMN lesion in upper limb and UMN lesion in lower limbs.*
- *When UMN lesion is associated with dorsal column lesion, it is suggestive of cervical myelopathy (other cause as above).*
- *If spastic paraplegia but no dorsal column lesion signs, causes may be other causes of cord compression.*

Q: What is myelopathy and radiculopathy?

A: As follows:

- Myelopathy: Compression of spinal cord due to any cause.
- Radiculopathy: Compression of exiting nerve root due to any cause.

Q: What is cervical myelopathy?

A: Cervical myelopathy is a condition caused by narrowing of spinal canal leading to compression of spinal cord.

Q: What are the causes of cervical myelopathy?

A: As follows:

- Cervical spondylosis.
- Cervical degenerative disc disease.
- Ossification of Posterior longitudinal ligament (OPLL).
- Cervical cord tumour.
- Epidural abscess.
- Trauma.
- Congenital stenosis.

Q: How to investigate?**A:** As follows:

- MRI of cervical spine.
- X-ray of cervical spine.
- CT scan may be done (useful to evaluate OPLL).

Q: How to treat?**A:** As follows:**Non-surgical:**

- Medications (NSAIDS, gabapentin, intra-articular steroid).
- Immobilization (hard collar in slight flexion).
- Physical therapy for neck strengthening, balance and gait training.
- Traction and chiropractic modalities are not likely to benefit and do have some risks.
- Be sure to watch patients carefully for progression.

Surgical:

- Anterior cervical discectomy/corpectomy and fusion.
- Posterior laminectomy and fusion.
- Posterior laminoplasty.
- Combined anterior and posterior procedure.
- Cervical disk arthroplasty.

Q: What is the prognosis?

A: Prognosis is variable. In many patients, the condition stabilizes or even improves without intervention. If progression results in sphincter dysfunction or pyramidal signs, surgical decompression should be considered.

Q: How to grade cervical myelopathy?**A:** According to NURICK scale:

Grade 0	Root symptoms only or normal
Grade 1	Signs of cord compression, normal gait
Grade 2	Gait difficulties but fully employed
Grade 3	Gait difficulties prevent employment, walks unassisted
Grade 4	Unable to walk without assistance
Grade 5	Wheelchair or bedbound

CEREBELLO-PONTINE (CP) ANGLE LESION

Instruction by the examiner:

- Examine the patient's cranial nerves.

Presentation of a Case:

- This patient has signs of Vth, VIth, VIIth **nerve lesion**. Also there is VIIIth **nerve lesion (perceptive deafness)**.
- There are signs of cerebellar lesion.
- There is nystagmus (cerebellar or vestibular).

My diagnosis is **Cerebello-pontine angle lesion**.

Q: What is the **commonest cause** of CP angle lesion?

A: Acoustic neuroma (vestibular schwannoma).

Q: What **else** do you want to see?

A: Fundoscopy.

Q: What are the **causes** of CP angle lesion?

A: As follows:

1. Acoustic neuroma.
2. Meningioma.
3. Others: Cholesteatoma, haemangioblastoma, granuloma, medulloblastoma, nasopharyngeal carcinoma, dermoid tumour, arachnoid cyst, basilar artery aneurysm, metastasis.

Q: How to **investigate**?

A: As follows:

- MRI (with Gadolinium contrast).
- CT scan (in some cases).
- Other tests: Pure tone audiometry.

Q: What are the **features** of acoustic neuroma?

A: Vertigo, progressive hearing loss, tinnitus.

Q: How to **treat**?

A: As follows:

- Surgical excision.
- Stereotactic radiotherapy (if surgery is not possible).

Q: What is **CP angle**? What are its **boundary, contents** and **relations**?

A: It is a triangular subarachnoid space that lies between the anterior surface of the cerebellum and the lateral surface of the pons.

Boundaries:

- Anterior: posterior surface of petrous temporal bone, including internal acoustic meatus.
- Posterior: anterior surface of cerebellum.
- Superior: inferior border of pons and cerebellar peduncle.
- Inferior: cerebellar tonsil.
- Medial: pons and inferior olive.

Contents:

- VIIth cranial nerve.
- VIIIth cranial nerve.
- Flocculus of the cerebellum.
- Foramen Luschka of 4th ventricle.
- Anterior inferior cerebellar artery (AICA).

Relations:

- Vth cranial nerve lies superior to this space.
- IXth, Xth and XIth cranial nerves lie inferior.
- The middle cerebellar peduncle is inferior.

RHEUMATOLOGY

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RHEUMATOLOGY

9

'The rheumatism is a common name for many aches and pains, which have yet got no peculiar appellation, though owing to very different causes'

—William Heberden

INTRODUCTION

Rheumatological diseases are commonly selected in any clinical examination. Of these, rheumatoid hand is quite common and also a very popular short case, though other cases are also common.

Most of the diagnoses are straightforward that can be easily diagnosed by looking at the patient or a particular part at a glance. It is frequently asked either to examine a particular part of the body or to look at a part for a spot diagnosis. However, even if asked to examine a particular part, examinee must look quickly from head to foot. A good clue for diagnosis may be obvious, such as systemic sclerosis, SLE, dermatomyositis and rheumatoid arthritis. During examination of joints, 'always look, feel, move, measure and compare with the other side'.

Common diseases selected for short case are:

- Rheumatoid hand.
- Systemic sclerosis.
- Ankylosing spondylitis.
- SLE.
- Chronic tophaceous gout.
- Dermatomyositis.
- Juvenile idiopathic arthritis (JIA).

Usual instructions by the examiner are:

- Look at the hands. What is your diagnosis? (may be rheumatoid hand, gangrene, gout, osteoarthritis, psoriatic arthritis).
- Examine the hands (as above).
- Look at the face (may be systemic sclerosis, butterfly rash in SLE, dermatomyositis).
- Palpate the skin (may be thickening in systemic sclerosis).
- Examine the lower limbs (may be sole and knee joints).

Remember some hallmarks in rheumatological disease, which indicates a particular diagnosis:

- Heberden's node in distal interphalangeal (DIP) joint and Bouchard's node in proximal interphalangeal (PIP) joint are hallmarks of primary osteoarthritis.
- Rheumatoid nodule is the hallmark of rheumatoid arthritis.
- Tophus is the hallmark of gout.
- Heliotrope rash and Gottron's sign are pathognomonic of dermatomyositis.
- Butterfly rash usually indicates SLE.
- Osteophyte (radiologically) is the hallmark of osteoarthritis.
- Syndesmophyte (radiologically) is the hallmark of ankylosing spondylitis.

SYSTEMIC SCLEROSIS

Instruction by the examiner:

- Look at the face. What are the findings? What else do you like to examine?
- Examine the hands or legs. What else do you like to examine?

Presentation of a Case (by Looking at the Face): Case No. 1

- The face is smooth, shiny, tight with hypopigmented and pigmented skin (salt and pepper appearance).
- Lips are thin, pursed with puckering.
- Nose is pinched up and tapered (beaking of nose, also called bird beak face).
- Loss of wrinkling of forehead and multiple telangiectasia (mention the location).
- Puckering of the skin around mouth and orifice of mouth is small (microstomia).
- The patient has difficulty in opening the mouth (ask to open the mouth).

My diagnosis is **Systemic sclerosis**.

Q: What else do you want to see?

A: I want to examine the skin of other parts of the body (see below), also hands, legs.



Face in systemic sclerosis



Flexion of fingers with skin change (typical hands in systemic sclerosis)



Infarction at the tip of the fingers with flexion contracture

N.B.: Combination of calcinosis, telangiectasia and sclerodactyly is called **CREST syndrome** (calcinosis, Raynaud's phenomenon, oesophageal involvement, sclerodactyly and telangiectasia) or **CRST syndrome** (calcinosis, Raynaud's phenomenon, sclerodactyly and telangiectasia). With these findings, mention the diagnosis as **CREST** or **CRST syndrome**.

Presentation of a Case (Hands): Case No. 2

- Skin of both hands are smooth, shiny, tight, thick and oedematous with pigmented and hypopigmented area.
- Interphalangeal joints are swollen with flexion contracture (or deformity, mention if any).
- There is sclerodactyly (tapering of fingers), infarction (or ulcer or gangrene) at the tip of finger with atrophy of pulp. May be resorption, beaking of the nails (pseudoclubbing due to resorption) and amputation of finger (may be).
- Telangiectasia at the base of nails.
- There is a hard nodule over one finger (calcinosis).

My diagnosis is **Systemic sclerosis**.

Q: In systemic sclerosis, what **questions** do you like to ask?

A: The following questions should be asked:

- Do your fingers change colour on exposure to cold? (Raynaud's phenomenon).
- If yes, what colours are they? (first, pallor, followed by cyanosis, then redness).
- Is there any difficulty in swallowing?
- Is there any difficulty in breathing?
- Is there any bowel abnormality? (occasional diarrhoea or constipation).

Presentation of a Case (by Looking and Palpating the Skin in Other Parts of the Body): Case No. 3

- Skin is pigmented, thick and tight. Also some vitiligo is present.

My diagnosis is **Systemic sclerosis**.

Q: What is **CREST** or **CRST** syndrome? What questions are asked in CREST syndrome?

A: It is a syndrome characterized by:

- **C:** Calcinosis.
- **R:** Raynaud's phenomenon.
- **E:** Oesophageal involvement (dysphagia).
- **S:** Sclerodactyly.
- **T:** Telangiectasia.

Ask about Raynaud's phenomenon and dysphagia. CREST syndrome is called limited cutaneous systemic sclerosis with better prognosis. Anti-centromere antibody is present in 70 to 80% cases (if diffuse deposition of calcium in subcutaneous tissue with presence of acrosclerosis, it is called Thibierge–Weissenbach syndrome).



Gangrene in multiple toes



Infarction of great toe



Infarction of 5th toe with amputation of great toe

Q: What is systemic sclerosis? What are the presentations?

A: It is a connective tissue disease characterized by fibrosis and degenerative changes in skin, blood vessels and internal organs. Common in females (F:M = 4:1), age 40 to 50 years. Usual presentations are:

- Raynaud's phenomenon—commonest (90 to 97%), may precede by months or years before other symptoms.
- Tightening and thickening of skin of hands and other parts of body, arthralgia, arthritis (non-erosive, inflammatory).
- GIT features: Heartburn (reflux oesophagitis due to hiatus hernia), dysphagia, odynophagia, occasional diarrhoea, constipation (called blind loop syndrome).
- Respiratory features: Shortness of breath (due to DPLD).

2 types:

- Diffuse cutaneous systemic sclerosis (DCSS, 30%): This involves the skin of face and trunk. Also above the knee and elbow (initially, skin is oedematous, thick and tight, several months later Raynaud's phenomenon may occur).
- Limited cutaneous systemic sclerosis (LCSS, 70%): This involves skin below the knee and elbow (initially, Raynaud's phenomenon, followed by skin change, also called CREST syndrome).

Other varieties (localized):

- Scleroderma sine scleroderma: Involves internal organ without skin lesion.
- Morphoea: Localized, well demarcated, indurated or plaqued, with central hypopigmentation and tethering of skin, usually in extremities and face.
- Linear: skin involvement is in a linear pattern, usually in lower limbs.

Q: What is the pathogenesis of systemic sclerosis?

A: As follows:

- Vascular change: damage in arteries, arterioles and capillaries. There is intimal proliferation, vessel wall inflammation and endothelial damage with release of cytokines and endothelin-I (causes vasoconstriction).
- Fibrotic change: Fibroblast synthesizes collagen I and III, fibronectin, glycosaminoglycans, causing fibrosis in dermis and internal organs.
- Humoral immunity: There is T-lymphocyte and complement activation, auto-immunity with antibody production to nuclear antigen.

Q: What are the histological findings of skin biopsy in systemic sclerosis?

A: As follows:

- Thinning or absence of epidermis.
- Excess collagen and fibrosis of dermis, loss of appendages in dermis, perivascular infiltration of chronic inflammatory cells (lymphocytes and plasma cells). Blood vessels show intimal proliferation and obliteration.

Q: What investigations should be done in systemic sclerosis?**A:** Diagnosis is clinical. The following investigations may be done:

1. CBC (ESR is high).
2. CRP (usually normal, may be high if severe organ involvement or co-existing infection).
3. Serology:
 - RA test (positive in 20 to 30% cases).
 - ANA (positive in 95% cases).
 - Anti-topoisomerase 1 or anti-Scl-70 (positive in 30% in diffuse type).
 - Anti-RNA polymerase (I, II and III) antibodies (20 to 25% in diffuse type). Associated with renal involvement.
 - Anti-centromere antibody (positive 60% in CREST, 10% in diffuse type) with speckled nucleolar pattern.
4. Skin biopsy for histopathology.
5. Others:
 - If renal involvement: serum urea, creatinine and electrolytes.
 - Urine R/E (may be proteinuria).
 - X-ray of hands (deposition of calcium in fingers, erosion, resorption of phalanges and disorganization of joints).
 - Chest x-ray (DPLD and honeycomb lung).
 - CT scan of the chest (to detect DPLD).
 - Lung function tests (shows restrictive lung disease).
 - Barium swallow (to see dysmotility or reduction of peristalsis, narrowing and dilatation. Hiatus hernia may be present, detected by barium swallow x-ray in Trendelenburg position).
 - Barium follow through.
 - Motility study may be done.
 - ECG.
 - IgG level (raised).

Q: What are the changes in the different systems of the body?**A:** As follows:

1. Skin changes:
 - In hands and face (see above).
 - Skin in other parts of the body (thick, tight, hyper or hypopigmented and vitiligo).
 - Skin of the chest is tight and thick (looks like **Roman breast plate**).
2. Joints and muscles: Flexion contracture or deformity. Proximal or distal muscle weakness.
3. Gastrointestinal:
 - Oesophagus: 50% involvement. May be reflux oesophagitis, sliding hiatus hernia, constriction or secondary achalasia, dysmotility or reduction of peristalsis. Oesophageal manometry shows abnormal and reduced peristalsis in 90%.
 - Stomach: Early satiety, gastric outlet obstruction, recurrent occult bleeding in stomach (**watermelon stomach**).
 - Intestine: Hypomotility, bloating, distension, intestinal obstruction or pseudo-obstruction, blind-loop syndrome, diarrhoea and wide mouth diverticula in colon. Rarely, a serious disorder called **pneumatosis cystoides intestinalis**, in which there is radiolucent cyst or streaks in the wall of small intestine due to air in the intestinal wall can occur (detected by plain x-ray abdomen). The patient presents with severe abdominal pain.

4. Liver: Primary biliary cirrhosis may be associated.
5. Respiratory:
 - DPLD, pulmonary hypertension and cor pulmonale. Pulmonary HTN may occur without parenchymal lung disease due to pulmonary vessel involvement. It is 6 times common in limited than diffuse type.
 - Others: Pneumonitis, rarely pleural effusion, alveolar cell carcinoma.
6. Heart: Dysrhythmia, conduction defect, heart failure, cardiomyopathy and pericardial effusion.
7. Kidneys (20% involvement):
 - Renal failure in advanced stage (often fatal).
 - Malignant hypertension (difficult to control, may respond to ACE inhibitors).
8. Endocrine:
 - Hypothyroidism (due to thyroid gland fibrosis).
 - Impotence.
9. Neurologic:
 - Entrapment neuropathy.
 - Facial nerve palsy.
 - Autonomic dysfunction.

N.B.: Systemic sclerosis may be associated as a part of mixed connective tissue disorder (SLE, RA, polymyositis). So, features of other disease should be looked for.

Q: How to manage systemic sclerosis?

A: No specific therapy, treatment is supportive and symptomatic.

1. General management for Raynaud's phenomenon:
 - Exposure to cold should be avoided (by use of gloves or mittens).
 - Lubricants should be used (to avoid dryness).
 - Smoking should be stopped,
 - Regular exercise and massage of skin,
 - Cleanliness of digital ulcer.
 - Drugs to be avoided (β -blocker, ergotamine, oral contraceptive and sympathomimetic).
 - Antiplatelet (aspirin) may be given.
 - Endothelin-1 receptor antagonist (bosentan) may be given.
 - Calcium antagonist (diltiazem, nifedipine), ACE inhibitor, angiotensin II receptor blocker (valsartan) may be used.
 - If no response or in severe case: prostacyclin analogue (epoprostenol) infusion intermittently.
 - If still no response: surgery (digital sympathectomy, microsurgical revascularization), lumbar sympathectomy, thoracic sympathectomy under video assisted thoracic surgery. If needed, amputation of fingers or toes.
 - Antibiotic: If infection. High dose should be given since tissue penetration is poor in systemic sclerosis.
2. For arthritis: NSAID. If synovitis is present, methotrexate may be given.

3. If myositis or alveolitis: Steroid and cytotoxic drugs may be used.
4. Other drugs, no proven benefit, but may be tried:
 - Penicillamine: reduces cross linking of collagen (acts as anti-fibrotic).
 - Methotrexate (given weekly, 7.5 to 15 mg).
 - Cyclosporine or interferon. Recombinant human relaxin (subcutaneously).
5. Other therapy, according to the involvement of the organ:
 - Physiotherapy.
 - If DPLD: cyclophosphamide or azathioprine combined with low dose steroid.
 - Hypertension: ACE inhibitor may be given.
 - Pulmonary hypertension: oral vasodilator, warfarin and oxygen. In advanced case, prostacyclin (inhaled, subcutaneous or IV) or oral endothelin-1 receptor antagonist (bosentan, sitaxentan) may be given.
 - Right heart failure: diuretic, digoxin. Heart lung or single lung transplantation in selected cases.
 - For reflux oesophagitis: proton pump inhibitor and prokinetic (domperidone, metoclopramide).
 - For blind loop syndrome: antibiotic.
 - If renal involvement: ACE inhibitor may be helpful.
 - Myositis: corticosteroid and cytotoxic drugs may be given.

Q: What is the role of steroid?

A: Little or no role in systemic sclerosis, can be given in low dose (10 mg/day) with cyclophosphamide in DPLD.

Q: What is the prognosis of systemic sclerosis?

A: Depends on type, age, sex, involvement of internal organ and extent of skin involvement. Bad prognostic factors are:

- Diffuse cutaneous systemic sclerosis.
- Elderly patient.
- Male sex.
- Involvement of internal organs (kidney, lung, heart).
- Proteinuria.
- High ESR.
- Low gas transfer of carbon monoxide.
- Pulmonary hypertension.

Limited cutaneous systemic sclerosis (CRST or CREST):

- Prognosis is relatively better.
- Usually mild.
- 70% show 10 year survival.
- Pulmonary hypertension may develop later on.

Diffuse type:

- 70% show 5 year survival.
- Death due to cardiac, renal and pulmonary involvement (commonest cause of death is renal failure).

Q: What are the **differential diagnoses** of systemic sclerosis or thickened skin?

A: Scleroderma like thickening of skin, secondary to other diseases is called **pseudoscleroderma**.

Causes are:

- Scleroedema.
- Scleromyxoedema.
- Eosinophilic fasciitis or eosinophilic myalgia syndrome.
- Amyloidosis.
- Graft versus host disease (GVHD).
- Diabetic cheiroarthropathy.
- Acromegaly.
- Porphyria cutanea tarda.
- Carcinoid syndrome.
- Toxic oil syndrome.
- Chemically induced (pentazocine, bleomycin, vinyl chloride).

EOSINOPHILIC FASCIITIS

Def: It is a scleroderma like syndrome characterized by pain, swelling, induration of skin and subcutaneous tissue followed by sclerosis of dermis and subcutaneous tissue. Features are:

- Skin is thick, but not tight.
- Common in adult, involves the skin of forearm and leg first, then peripheral parts.
- No Raynaud's phenomenon and no internal organ involvement.
- Carpal tunnel syndrome is an early feature, more marked after exercise.
- Associated with eosinophilia, hypergammaglobulinaemia, thrombocytopenia, aplastic anaemia, myelodysplastic syndrome.

Microscopical examination of skin in eosinophilic fasciitis shows:

- Marked fibrosis of subcutaneous fascia.
- Infiltration of inflammatory cells.
- Infiltration of plenty of eosinophil.

Treatment:

- Usually self limiting, spontaneous resolution may occur in 2 to 5 years.
- Good response to steroid.
- H₂ receptor blocker or proton pump inhibitor.
- Diet containing L-tryptophan should be avoided.

SCLERODEMA

- It is a disease characterized by painless, oedematous induration of face, scalp, neck, trunk and upper part of the extremities.
- The term scleroedema is a misnomer because neither sclerosis nor oedema is found on microscopic examination.
- There is no involvement of the hands and feet.
- Common in children.
- May be associated with streptococcal infection, blood dyscrasia or diabetes mellitus.
- Usually self limiting, resolves in 6 to 12 months, sometimes persistent. It is typically considered benign, but it can involve internal organs and rarely may result in death.
- There is no specific treatment. Only symptomatic and supportive.

RAYNAUD'S PHENOMENON OR DISEASE

Instruction by the examiner:

- Look at the hand. What are the findings? What is your diagnosis?

Presentation of a Case (Hands):

- The fingers are pale, some are cyanosed and cold.
- There is sclerodactyly (tapering of fingers), infarction (or ulcer or gangrene) at the tip of finger and atrophy of pulp. May be resorption, beaking of the nails (pseudoclubbing due to resorption) and amputation of finger (mention if any).

My diagnosis is **Raynaud's disease**.

Q: What is the **commonest cause**?

A: Systemic sclerosis.



Pallor on exposure to cold
(dorsal aspect)



Pallor on exposure to cold
(palmar aspect)



Cyanosis at the tip of fingers

Q: What is **Raynaud's phenomenon**?

A: Raynaud's phenomenon is a syndrome of episodic digital ischaemia manifested by pallor, cyanosis, redness of the fingers and toes on exposure to cold. Vibration and emotional activity may precipitate the attack. It is due to episodic vasoconstriction or vasospasm of small arteries, arterioles and capillaries of fingers and toes.

Q: What are the **signs** of Raynaud's phenomenon?

A: 3 signs or stages (remember **PCR**):

- First: **Pallor** (due to vasoconstriction of peripheral arterioles).
- Second: **Cyanosis** (due to deoxygenated blood following ischaemia).
- Last: **Redness** (due to reactive hyperaemia, there is increased blood flow after vasodilatation).

Q: What are the mechanisms of Raynaud's phenomenon?**A:** As follows:

- Exaggerated reflex sympathetic vasoconstriction (Raynaud's original theory).
- Abnormalities in the vascular wall resulting in hyper-responsiveness and vasoconstriction to cold.
- Recent opinion suggests that accelerated destruction of platelet and release of agents such as serotonin and thromboxane A₂ causes vasoconstriction in some patients with Raynaud's phenomenon.

Q: What is Raynaud's disease and Raynaud's syndrome?**A:** As follows:

- When the disease is primary, it is called Raynaud's disease.
- When the disease is secondary to other disease, it is called Raynaud's syndrome.

Q: What are the differential diagnoses of Raynaud's phenomenon?**A:** As follows:

- Acrocyanosis.
- Erythromelalgia.
- Chilblain.
- Cold agglutinin disease.

Q: What are the causes?**A:** As follows:

1. Primary or idiopathic: Also called Raynaud's disease (50 to 60%).
 - Five times more common in females than in males.
 - Usually in young patients, 20 to 40 years of age, may be associated with angina.
 - Thumbs often spared. Usually runs benign course.
2. Secondary causes:
 - Systemic sclerosis (common cause).
 - Collagen disease (SLE, mixed connective tissue disease, RA, dermatomyositis, Sjögren's syndrome).
 - Occupation (pneumatic drills, vibrating tools).
 - Obliterative arterial disease (atherosclerosis, Buerger's disease).
 - Drugs (beta-blocker, ergotamine, cytotoxic drug: vinblastine, bleomycin and cisplatin).
 - Neurogenic (cervical rib, spinal cord disease).
 - Haematological (cryoglobulinaemia or cold agglutinin disease, myeloproliferative disease, Waldenstrom's macroglobulinaemia).

Q: How to treat Raynaud's disease?**A:** See above (in systemic sclerosis).

N.B.: Women who develop toxæmia of pregnancy are more likely to have history of Raynaud's disease.



Infarction at the tip of fingers,
pulp atrophy



Cyanosis of toes



Infarction of great toe

RHEUMATOID HAND

Instructions by the examiner:

- Examine the hands of this patient. Or, look at the hands. What is the likely diagnosis?

Proceed to examine the hands as follows: (First, look at the dorsum and palm of hands, then proceed).

Inspection: (There is bilateral, symmetrical polyarthropathy). Look carefully the following points:

1. Generalized wasting involving thenar, hypothenar and all small muscles of the hand with dorsal guttering in both hands.
2. Any ulcer, infarction, gangrene, rash, rheumatoid nodule and palmar erythema (mention, if present).
3. Joints of hands:
 - Flexion deformity or contracture (involving all the fingers).
 - PIP: spindle shaped swelling and boutonniere deformity (involving all the fingers or mention which fingers).
 - DIP: swan neck deformity (involving all the fingers or mention which fingers).
 - Z deformity of thumb (right or left or both, mention accordingly).
 - Ulnar deviation and dorsal subluxation of ulna at the carpal joint (right or left or both hand).
4. Wrist joint: any swelling, synovial thickening and subluxation.
5. Ask the patient to make apposition of both hands (prayer sign), flex and extend the fingers (see any deformity).

Palpation:

1. Ask the patient, if any pain in hands (be careful not to hurt).
2. Palpate the joints to see any tenderness.
3. Feel for rheumatoid nodule on palmar surface (head of metacarpals), dorsal surface of fingers (also see in extensors of forearm, elbow, occiput, scapula, shin and Achilles tendon).
4. Neurological examination of hands (see in the chapter of 'examination of hands').
5. Finally, assess the functional activity of hands: Ask the patient to use a glass and drink, open the button, write with a pen, grip strength (ask to squeeze your fingers), key grip (give a key, ask the patient to move the hand with the key, like unlocking).

Q: At this point, the examiner may ask, 'What else do you like to see?'

A: I want to examine other joints, eyes, chest and abdomen to see extra-articular manifestations.

Presentation of Case No. 1 (Rheumatoid Hand):**1. Inspection:**

- There is generalized wasting of small muscles of hands with dorsal guttering. No ulcer, infarction, gangrene or rash.
- Both wrist joints are swollen with restricted movements.
- PIP joints of both hands are spindle shaped. There is swan neck deformity in right little and left ring fingers, Z deformity in both thumbs and ulnar deviation of right hand with dorsal subluxation of ulnar styloid.
- Movement is restricted in wrists and fingers of both hands with slightly impaired functional activity.

2. Palpation:

- All the joints of both hands are tender.
- Synovial thickening is present in both wrists.
- There is a rheumatoid nodule in the extensor surface of right forearm.

My diagnosis is **Rheumatoid arthritis**.

Q: Could it be **sero-negative arthritis** or **ankylosing spondylitis**?

A: Unlikely, since in sero-negative arthritis, there is usually asymmetrical involvement of bigger joints. But in this case, there is bilateral symmetrical involvement of small peripheral joints.



Swan neck deformity (DIP)



Boutonniere deformity (PIP of ring and little finger)



Z-deformity of thumb, ulnar deviation and swan neck deformity

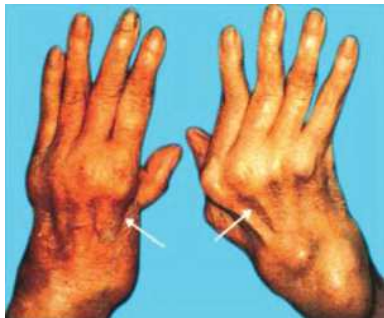
Q: Which joint is **spared** in hand in RA?

A: Distal interphalangeal joint (may be involved in secondary osteoarthritis).

Presentation of Case No. 2 (Vasculitis):

- Mention as above.
- There is a small ulcer and few infarctions at the tip of fingers and toes (mention which one).
- Radial pulse is feeble in both sides.

My diagnosis is Rheumatoid arthritis with vasculitis.



Severe rheumatoid arthritis
(Dorsal guttering)



Vasculitis in rheumatoid
arthritis



Vasculitis in rheumatoid hand

Presentation of Case No. 3 (Foot):

- All the metatarsophalangeal joints and interphalangeal joints are swollen and deformed in both feet.
- Lateral deviation with dorsal subluxation of toes.
- Plantar subluxation of the metatarsal head.
- Hallux valgus deformity.
- Feet are flat with plantar erythema.

My diagnosis is **Rheumatoid arthritis**.

READ THE FOLLOWING TOPICS IN RELATION TO RHEUMATOID ARTHRITIS

Q: What is RA?

A: It is a chronic autoimmune inflammatory destructive and deforming polyarthritis characterized by bilateral symmetrical involvement of small and large joints with systemic and extra-articular features with exacerbations and remissions. Age 30 to 50 years, common in females. Before menopause, it is 3 times more in female than male, but after menopause, sex ratio is almost equal.

Q: What are the mechanisms of wasting of muscles in RA?

A: Multiple factors are responsible: disuse, vasculitis, polyneuropathy, mononeuritis multiplex and entrapment neuropathy.

Q: What is boutonniere deformity? What is the mechanism?

A: Fixed flexion of PIP joint and extension of DIP joint. Because of chronic synovitis of PIP joint, there is rupture of central slip of extensor tendon, allowing to protrude the joint between two lateral slips of extensor tendon.

Q: Why it is called boutonniere or button-hole?

A: Because of rupture of central slip of extensor tendon, it looks like gap of button hole.

Q: What is swan neck deformity? What are the mechanisms?

A: Fixed flexion of DIP joint and extension of PIP joint (reverse of boutonniere). **Mechanism:** Because of chronic synovitis:

- Rupture or stretching of extensor tendon on dorsum of DIP joint.
- Secondary to stretching of volar plate at PIP joint.
- Shortening of intrinsic muscles of hands, which exerts tension on dorsal tendon sheath causing hyperextension of PIP joint.

Q: Why radial deviation?

A: Weakness of extensor carpi ulnaris leads to radial deviation at wrist as the carpal bone rotates.

Q: Why ulnar deviation?

A: It occurs in response to radial deviation to keep the tendons to the phalanges in normal alignment to the radius.

Q: Why Z deformity of thumb?

A: Due to chronic synovitis, there is hyperextension of IP joints with fixed flexion and subluxation of MCP joints of thumb.



Severe rheumatoid arthritis



Baker's cyst (Bilateral)



Baker's cyst
(unilateral)



Rheumatoid nodule
(forearm)

Q: What is Baker's cyst?

A: Cyst on the back of knee joint, communicates with the joints but fluid is prevented from returning to the joint by a valve like mechanism. May rupture during knee flexion and fluid enters into the calf. After rupture, there is severe pain, swelling and tenderness in the calf. It may be confused with deep venous thrombosis.

Diagnosis: USG of knee joint, CT scan or MRI and arthrogram may be done. Treatment after rupture of Baker's cyst:

- Relief of pain by NSAID.
- Elevation of the limb.
- Intra-articular injection of steroid (methylprednisolone or triamcinolone).
- Surgery may be necessary.

Q: What are the causes of Baker's cyst?

A: Rheumatoid arthritis, osteoarthritis and rarely congenital.

Q: What is rheumatoid nodule? Where is it found?

A: These are painless, firm, subcutaneous nodule, invariably associated with positive rheumatoid factor. It is present in 20 to 30% cases of rheumatoid arthritis.

Sites: Pressure points such as elbow, extensor surface of forearm and hands (fingers), scapula, scalp, sacrum, shin, Achilles tendon, toes, sclera, pleura, lungs and pericardium.

Significance of rheumatoid nodule:

- Associated with high titre of rheumatoid factor (positive RA test).
- Associated with active and aggressive RA.
- A bad prognostic sign.

Histologically, it shows 3 zones:

- Central zone of necrosis containing collagen fibril, noncollagen filament and cellular debris.
- Mid zone of palisading macrophages.
- Outer zone of granulation tissue.

Nodules may ulcerate and become infected. Treatment with methotrexate may increase the number of rheumatoid nodule in some patients. Nodules resolve when the disease is under control. If causes pain, it may be removed surgically or by local injection of corticosteroid.

Differential diagnosis of nodule:

- Rheumatoid nodule.
- Tophi of gout.
- Xanthomata.
- Olecranon bursa in elbow.
- Sarcoid nodule.
- Neurofibroma

Q: What are the bad or poor prognostic factors of RA?

A: As follows:

1. Clinical:

- Insidious rather than explosive onset.
- Early development of rheumatoid nodule.
- Extra-articular manifestations.
- Severe functional impairment.
- One year active disease without remission.
- Increasing number of peripheral joints involvement.
- Severe disability at the onset.
- Female sex.

2. Blood tests:

- High titres of ACPA (anti-CCP) antibodies and rheumatoid factor.
- High CRP.
- Normochromic normocytic anaemia.

3. X-rays:

- Early erosion and damage.

N.B.: Ultrasound and MRI can show cartilage and bone damage prior to conventional X-rays.

Q: What are the **diagnostic criteria** of RA?

A: ACR/EULAR 2010 criteria for rheumatoid arthritis:

Criteria	Points
1. Joint involvement • 1 medium to large joint • 2–10 medium to large joints • 1–3 small joints (large joints not counted) • 4–10 small joints (large joints not counted) • >10 joints; at least one small joint	0–5 0 1 2 3 5
2. Serology • Negative RF and negative ACPA • Low positive RF or low positive ACPA • High positive RF or high positive ACPA	0–3 0 2 3
3. Acute-phase reactants • Normal CRP and normal ESR • Abnormal CRP or abnormal ESR	0–1 0 1
4. Duration of symptoms • <6 weeks • ≥6 weeks	0–1 0 1

Patients with ≥6 points are diagnosed as definite RA. If they have both typical erosions and long-standing disease, they can also be classified as RA.

Q: What is **malignant RA**?

A: Severe and progressive RA associated with severe extra-articular manifestations, systemic features and vasculitis.

Q: What are the **mechanisms of anaemia** of RA?

A: As follows:

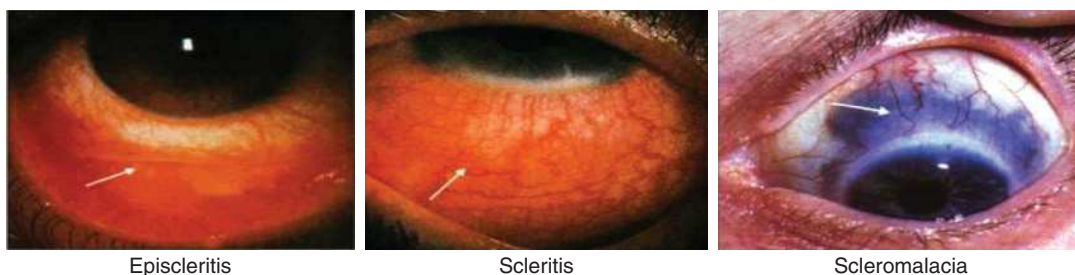
- Anaemia of chronic disorder.
- Megaloblastic anaemia (due to either folate deficiency or if associated with pernicious anaemia).
- Hypersplenism (in Felty's syndrome).
- Autoimmune haemolytic anaemia (Coomb's test may be positive).
- GIT bleeding (due to NSAIDs or vasculitis, causing iron deficiency anaemia).
- Marrow suppression (due to methotrexate, sulphasalazine).

Q: What are the **extra-articular** manifestations of RA?

A: As follows:

1. Eye:
 - Episcleritis.
 - Scleritis.
 - Scleromalacia.
 - Scleromalacia perforans.
 - Keratoconjunctivitis sicca.

2. Respiratory:
 - Pleurisy.
 - Pleural effusion (may be bilateral).
 - Fibrosing alveolitis (DPLD).
 - Nodules in the lungs (Caplan's syndrome).
 - Obliterative bronchiolitis (rare).
3. Cardiac:
 - Pericarditis (30%).
 - Pericardial effusion (rare).
 - Chronic constrictive pericarditis (rare).
 - Rarely myocarditis, endocarditis, heart block, arrhythmia, cardiomyopathy, aortic regurgitation, coronary artery occlusion causing IHD.
4. Vasculitis: Digital arteritis and nail fold infarction, Raynaud's phenomenon, visceral arteritis, mononeuritis multiplex, pyoderma gangrenosum.
5. Neurological:
 - Entrapment neuropathy (compression of nerves by hypertrophic synovium), commonly carpal tunnel syndrome (due to compression of median nerve) and tarsal tunnel syndrome (due to compression of posterior tibial nerve).
 - Peripheral neuropathy.
 - Mononeuritis multiplex.
 - Cervical cord compression (due to atlanto-axial subluxation).
 - Progressive cervical myelopathy.
6. Haematological:
 - Anaemia: Usually normocytic normochromic, occasionally macrocytic due to folate deficiency or associated with pernicious anaemia and microcytic hypochromic due to bleeding from NSAIDs.
 - Thrombocytosis.
 - Eosinophilia.
 - Pancytopenia (due to hypersplenism in Felty's syndrome).
7. Musculoskeletal:
 - Muscle wasting.
 - Tenosynovitis.
 - Bursitis.
 - Osteoporosis.
8. Others:
 - Lymphadenopathy.
 - Splenomegaly.
 - General features (malaise, fever, weakness, weight loss, wasting).
 - Amyloidosis.



Episcleritis

Scleritis

Scleromalacia

Q: What is rheumatoid factor?

A: Rheumatoid factor is an antibody, directed against Fc portion of IgG. It may be IgM or IgG type. Rheumatoid factor is positive in 75% cases, but 100% positive in RA with extra-articular manifestations. It is detected by latex slide test (RA test is more sensitive, but less specific and is used for screening) and Rose–Waller test (RW test, sheep cell agglutination test, is less sensitive, but more specific). Other causes of positive rheumatoid factor are:

- Collagen diseases: Sjögren's syndrome (90%), SLE (30%), systemic sclerosis, polymyositis or dermatomyositis, JIA, idiopathic fibrosing alveolitis and mixed essential cryoglobulinaemia.
- Infections: Infectious mononucleosis, infective endocarditis, tuberculosis, leprosy, kala-azar, hepatitis B, syphilis, malaria, filariasis and schistosomiasis.
- Liver disease: PBC (50%).
- Sarcoidosis.
- Temporarily after vaccination and blood transfusion.
- Over 65 years (20% in normal population).

High titres of rheumatoid factor indicate:

- Severe erosive disease.
- More extra-articular manifestations.
- Poor prognosis.
- Associated with rheumatoid nodule, vasculitis and Felty's syndrome.

Q: What is palindromic RA?

A: Recurrent acute episode of monoarthritis lasting 24 to 48 hours. Knee and finger joints are commonly affected, but any peripheral joint may be involved. Fever may occur, but no other systemic features. It may be confused with acute gouty arthritis and atypical onset of rheumatoid arthritis. There may be many attacks without any permanent articular damage. However, one third to half cases may develop typical RA. This can be treated with NSAIDs during pain. Hydroxychloroquine may be used in preventing recurrent attack.

Q: What is Caplan's syndrome?

A: Rheumatoid lung nodules with pneumoconiosis is called Caplan's syndrome. Common in coal-workers' pneumoconiosis, may occur in any pneumoconiosis. Nodules are rounded, 0.5 to 2.5 cm, present at periphery of the lung. These may rupture causing pneumothorax or may cavitate and cause haemoptysis. It may be confused with tuberculosis or neoplasm.

Q: What is Felty's syndrome?

A: Rheumatoid arthritis with splenomegaly and neutropenia is called Felty's syndrome. There may be hypersplenism (anaemia, leucopenia and thrombocytopenia). It occurs in long-standing, seropositive, deforming, but inactive arthritis, in <1% cases of RA. Females are affected more than males, age 50 to 70 years. Leg ulcers, sepsis or frequent infection of skin and respiratory tract are common due to neutropenia. Splenectomy may be necessary for hypersplenism. It is associated with high titre of rheumatoid factor, subcutaneous nodules and other manifestations of systemic rheumatoid disease. Complications like splenic rupture, severe life threatening infection or toxicity due to immunosuppressants may occur.

Q: What precaution is necessary before general anaesthesia or upper GI endoscopy?

A: X-ray of cervical spine should be done to exclude atlanto-axial subluxation (otherwise during anaesthesia, cervical cord compression may lead to sudden death).

Q: If the patient develops nephrotic syndrome (or proteinuria in urine examination), what is the likely cause?

A: Renal amyloidosis.

Q: What investigations are done in RA?

A: As follows:

- CBC (ESR is high, pancytopenia may occur in Felty's syndrome).
- RA test and RW test.
- ACPA (anti citrullinated protein antibody).
- X-ray of hands and other involved joints, chest X-ray.
- Others: CRP (high) and urine analysis (proteinuria, may occur in amyloidosis).

Q: What is Anti-citrullinated protein antibody (ACPA, previously called anti-CCP antibody)? What is its significance?

A: It is the antibody to cyclic citrullinated peptide (CCP). It binds to peptides (citrullinated antigens, vimentin, fibrinogen, alpha enolase and type II collagen) in which the amino acid arginine is converted to citrulline by peptidylarginine deaminase, an enzyme abundant in inflamed synovium. Anti-CCP antibody is highly specific in RA (90%), present in 80% patients with rheumatoid arthritis. Unlike rheumatoid factor, it is not positive in other autoimmune diseases. It is helpful for early diagnosis and is also a predictor of aggressive disease. In patient with undifferentiated arthritis, ACPA is helpful for early diagnosis in RA. It may be detected in asymptomatic patient several years before the development of RA.

Q: How to treat RA?

A: As follows:

- Relief of symptoms by rest and NSAID. Also intra-articular injection, splinting, hydrotherapy may relieve symptoms.
- Suppression of activity and progression of disease by disease modifying anti-rheumatic drug (DMARD).
- Other measures: Physiotherapy, orthopaedic measures. Synovectomy of the wrist or finger tendon sheaths of hands may be required for pain relief or to prevent tendon rupture if failure to medical therapy. Osteotomy, arthrodesis or arthroplasty may be needed later.
- Patient's education is important.

Q: What are the surgical treatment in RA?**A:** As follows:

- Synovectomy of wrist or finger tendon sheath (for pain relief or tendon rupture).
- In advanced or severe cases: arthrodesis, arthroplasty, osteotomy may be done in selected cases.

Q: What DMARDs are used?**A:** As follows:

- First choice: sulphasalazine, methotrexate.
- Other drugs: Chloroquine, hydroxychloroquine, leflunomide, azathioprine, cyclosporine.
- Biological therapy: Anti-TNF-alpha and anti IL-1, rituximab are more effective than other DMARD in preventing joint erosions. If disease activity persists after use of two DMARDs, biological therapy should be considered.
- DMARD should be started from the beginning, may take 4 to 12 weeks for response. If no effect in 6 to 12 weeks, combination of methotrexate and sulphasalazine may be given. Prednisolone 7.5 to 10 mg may be added.

BRIEF NOTES ABOUT DMARDs**Sulphasalazine:**

- Mode of action: When taken by mouth, it is broken to sulphapyridine and 5-aminosalicylic acid (ASA). Sulphapyridine is effective in RA (ASA is effective in inflammatory bowel disease). It acts probably by inhibiting cyclo-oxygenase and other enzymes responsible for synthesis of prostaglandin.
- Dose: Start with low dose, increase the dose weekly. Initially, 250 mg (½ tablet) BID for 1 week. Then 500 mg (1 tablet) BID for 1 week. Then 1,000 mg (2 tablets) BID, to be continued (maximum dose 2 to 3 gm daily).
- Side effects: GIT upset (anorexia, nausea, vomiting, diarrhoea), skin rash, Stevens Johnson syndrome, reversible sterility in males, blood dyscrasias (agranulocytosis, megaloblastic anaemia and haemolytic anaemia).
- Periodic check up: CBC, liver function test (SGPT) and renal function tests (S. creatinine), every 1 to 3 months.

Methotrexate:

- Very effective DMARD. May take 4 to 6 weeks to act. Dose: 7.5 to 10 mg, in a fixed day weekly (up to 25 mg). Folic acid 5 mg/day should be given on the next day (folinic acid is more preferable).
- Side effects: Anorexia, nausea, vomiting (prevented by using anti-emetic before starting the drug), mouth ulcer. Rarely, may cause bone marrow depression. Prolong use may cause hepatic fibrosis and DPLD.
- Periodic check up: CBC, liver function tests (SGPT) and renal function test (S. creatinine) should be done.
- Mechanism of action: Inhibits dihydrofolate reductase, interfering with DNA synthesis and cell division.
- Initial pneumococcal and annual influenza vaccinations are given.
- Should not be used in pregnancy and conception should be delayed until women have been off the drug for 6 weeks.

Chloroquine:

- It has a weak with slow DMARD effect. Dose: 250 mg daily as a single dose.
- Side effects: Anorexia, nausea, vomiting, skin rash. Prolonged use may cause neuro-myopathy and ocular toxicity. In eye, corneal microdeposit (reversible after drug withdrawal), retinopathy (may cause blindness), bull's eye macula, optic neuritis. Periodic eye examination is essential. To reduce ocular toxicity, drug is given for 10 months in a year.

Hydroxychloroquine:

- Dose: 200 to 400 mg daily. Used alone in mild disease or as an adjuvant with other DMARD.
- Retinopathy is a serious complication, but this is rare before 6 years of treatment.

Leflunomide:

- If no response to MTX, it can be used alone or with MTX. Dose: 100 mg daily for 3 days, then 10 to 20 mg daily.
- Side effects: Skin rash, diarrhoea, reversible alopecia, hepatotoxicity, carcinogenic and teratogenic. It needs a washout of 2 years before conception (3 months in man and 2 years in woman), so avoid in women who want to be pregnant.
- Periodic blood check up is mandatory.

Biological agents: These agents block specific immune factors responsible for RA. These are very expensive, used only when failure of two DMARDs. Important biological agents are as follows:

Anti-TNF α :

1. It is more effective, rapid onset of action, greater clinical efficacy and sustained benefit than standard DMARD.
2. Anti-TNF drugs are:
 - Infliximab (given in infusion every 1 to 2 months). Should be given in combination with methotrexate.
 - Etanercept (given SC every week). It is a decoy receptor for TNF- α .
 - Adalimumab (given SC every 2 weeks).
 - Other new drugs: Certolizumab (given SC every 2 weeks), Golimumab (given SC every 4 weeks).
3. Side effects: Hypersensitivity, headache, hypotension, reactivation of latent tuberculosis. Rarely, lymphoma may occur.

Anti-interleukin (IL-1) receptor: Anakinra may be used in RA when anti-TNF α is unsuccessful (less effective than anti-TNF). It is used in combination with methotrexate.

Anti-interleukin 6 (IL-6) receptor: Tocilizumab. It is a humanized monoclonal antibody against IL-6 receptor. It is used for treatment of moderate to severe active rheumatoid arthritis in adult, alone or in combination with methotrexate and/or other DMARDs. Dose 8 mg/kg as IV infusion, once in every 4 weeks.

Rituximab:

- It is an antibody directed against CD-20 receptor, expressed on B lymphocytes and immature plasma cell.
- It produces significant improvement in RA positive patients. May be used alone or with steroid or methotrexate.
- It is given by two IV infusions (1 gm each) 2 weeks apart.

Abatacept: It is an inhibitor of T cell activation.

Tofacitinib: It is an oral JAK 3/1 receptor inhibitor.

Q: What are the criteria to see remission or response to therapy of RA?

A: ACR/EULAR definitions for disease remission at any time point, patient must satisfy all of the following:

- Tender joint count ≤ 1 .
- Swollen joint count ≤ 1 .
- C-reactive protein ≤ 1 mg/dL.
- Patient global assessment ≤ 1 (on a 0 to 10 visual analogue scale).

OR,

- At any time point, patient must have a Simplified Disease Activity Index score of ≤ 3.3 .

Q: What are the differences between rheumatic fever and rheumatoid arthritis?

A: As follows:

Points	Rheumatic Fever	RA
1. Age	5 to 15 years	20 to 40 years
2. Cause	Sequelae of immune response to <i>Streptococcus</i> beta-haemolyticus sore throat	Autoimmune
3. Joints involved	Large	Peripheral small joints
4. Type of arthritis	Fleeting	Bilateral, symmetrical
5. Diagnosed by	2 major or 1 major and 2 minor criteria plus signs of previous <i>Streptococcus</i> infection	According to ACR/EULAR criteria
6. Morning stiffness	Absent	Present
7. RA, ACPA test	Negative	Positive
8. Subcutaneous nodule	Present	Rheumatoid nodule
9. Erythema marginatum	Present	Absent
10. Joint deformity	Absent	Present
11. Cardiac involvement	Common	Less
12. Chronic constrictive pericarditis	Never	May cause
13. Chorea	May be present	Absent
14. Treatment	Prophylactic penicillin	DMARD
15. Sequelae	Rheumatic valvular lesion (it licks the joints, kills the heart)	Not so

BRIEF NOTE ABOUT SJÖGREN'S SYNDROME

Definition: It is an autoimmune disorder characterized by dryness of eye (keratoconjunctivitis sicca) and dryness of mouth (xerostomia) with non-erosive arthritis. Fibrosis and atrophy of salivary

glands occur. There is infiltration of lymphocytes and plasma cells in lacrimal and salivary glands. It is of 2 types:

- Primary: Not associated with collagen disease (also called sicca syndrome).
- Secondary: Associated with collagen disease (commonly RA).

Clinical features of primary Sjögren's syndrome: common in females, F:M = 9:1, 40 to 50 years.

- Dryness of mouth and eyes.
- Arthralgia and non-progressive arthritis.
- Raynaud's phenomenon.
- Dysphagia.
- In lung: pulmonary diffusion defect and fibrosis.
- Renal: renal tubular acidosis, nephrogenic diabetes insipidus.
- Vasculitis.
- Other features: fever, weakness, lymphadenopathy, neuropathy, fit, depression.
- Lymphoma: increased incidence of non-Hodgkin's B cell lymphoma (It is associated with 40-fold risk).
- May be associated with other autoimmune disease (e.g., thyroid disease, myasthenia gravis, PBC, autoimmune hepatitis).

Investigations:

1. CBC (high ESR).
2. Schirmer's test (a strip of filter paper is placed inside lower eyelid. If it is <10 mm in 5 minutes, it indicates defective tear production).
3. Biopsy of lip or salivary gland (shows lymphocytic and plasma cell infiltration).
4. Rose Bengal staining of eyes shows punctate or filamentary keratitis.
5. Antibody test:
 - RA test (positive in 90%).
 - ANA (positive in 80%).
 - Anti-Ro (SS-A, positive in 60 to 90%). It can cross placenta causing congenital complete heart block in newborn baby).
 - Anti-La (SS-B).
 - Anti-mitochondrial antibody (positive in 10%).

Treatment:

- Artificial tear (hypromellose), contact lens, oral hygiene, artificial saliva, oral gel and chewing gum.
- Stimulation of saliva flow by sugar free chewing gum or lozenges may be helpful.
- Oral candidiasis should be treated promptly.
- Vaginal dryness is treated with lubricants such as K-Y jelly.
- Hydroxychloroquine (2 to 3 mg/kg daily, may improve the flow of tear).
- Treatment of the primary cause.
- Extra-glandular, MSK, persistent salivary gland swelling, neuropathic manifestations may respond to steroid.
- Immunosuppressive drugs can be added.

KNEE JOINT ARTHRITIS (EXAMINATION OF KNEE JOINT)

Instruction by the examiner:

- Examine the knee joints. Or, examine the lower limbs. What are your findings?

Proceed as follows: (With permission, expose the lower limbs, patient is lying in supine position. Look carefully both front and back of knee. If obvious finding is arthritis, examine the joints. If nothing obvious, perform neurological examination).

Inspection:

- Obvious joint swelling (right or left or both, localized or generalized).
- Deformity of the joint.
- Skin (red, shiny, pigmentation, scar mark).
- Back of knee (Baker's cyst).
- Wasting of muscles of thigh or leg, swelling in calf (may be due to rupture of Baker's cyst).

Palpation:

- Feel the temperature (compare with normal side).
- Tenderness.
- Synovial thickening (in supra-patellar part).
- Examine for effusion as follows:
 - Patellar tap (fluid from supra-patellar bursa is forced into the joint space by squeezing the lower part of quadriceps. Then patella is pushed posteriorly by tip of two or three fingers).
 - If small effusion, see **Bulge sign** (left hand compresses the supra-patellar pouch at the lower end of quadriceps and index finger of right hand is run along the groove on either side of patella alternately. If bulging is present due to small effusion, it will not be compressed).
- See the movement passively, ask if any pain. See the range of movement and feel for any crepitus.
- Now examine the ligaments:
 - Medial and lateral collateral ligaments: By flexing the knee and holding the leg with one hand, palpate with other hand in lateral and medial movement of leg.
 - Cruciate ligaments: Flex the knee at 90°, then sit over the foot of the patient lightly to fix the leg. Now pull and push the leg anteriorly and posteriorly by keeping the fingers on the back of knee and feel the ligaments. Increased anterior movement of leg suggests anterior ligament laxity and increased posterior movement of leg suggests posterior ligament laxity.

Presentation of a Case (Suppose Painful Left Knee Joint with Effusion): Case No. 1

- The left knee joint is swollen, more marked above the patella. Skin is red and shiny. There is a cystic swelling on the back of right knee (Baker's cyst).
- Local temperature is raised and the joint is tender.
- Patellar tap is positive (indicates effusion). There is restricted movement of left knee.

My differential diagnoses are (mention the causes according to age):

In young patient, the causes are:

- Traumatic.
- Infective arthritis (pyogenic, tuberculous).
- Juvenile idiopathic arthritis (JIA).
- Reactive arthritis or Reiter's syndrome.
- Haemophilic arthritis.
- Other seronegative arthritis (such as ankylosing spondylitis, psoriatic arthritis).

In middle aged or elderly patient, the causes are:

- Traumatic.
- Infective arthritis (pyogenic, tuberculous).
- Gout.
- Pseudogout.
- Reactive arthritis.
- Osteoarthritis.
- Rheumatoid Arthritis.



Knee swelling (left)



Knee swelling (bilateral)

Presentation of a Case (Suppose both Knee Joints): Case No. 2

- Both knee joints are swollen, left one is more than the right. Then, describe as above in both knee joints.

My differential diagnoses are (mention according to the age):

In young patient, the causes are:

- Rheumatic fever (if deformity, it is **against** rheumatic fever).
- Reactive arthritis or Reiter's syndrome.
- Juvenile idiopathic arthritis (JIA).
- Seronegative arthritis (such as ankylosing spondylitis, enteropathic arthritis).
- Rheumatoid arthritis.
- Psoriatic arthritis (check for skin lesions and nail change).

In middle aged or elderly patient, the causes are:

- Osteoarthritis.
- Gout.
- Pseudogout.
- Rheumatoid arthritis.
- Psoriatic arthritis.
- Seronegative arthritis (such as ankylosing spondylitis, enteropathic arthritis).

Q: How will you investigate this patient?

A: As follows:

1. CBC with ESR (shows leucocytosis in septic arthritis. ESR may be high).
2. CRP (may be high).
3. X-ray of knee joint.
4. ACPA, RA test (to exclude rheumatoid arthritis).
5. Serum uric acid.
6. Aspiration of joint fluid and analysis:
 - Physical character (straw, purulent or haemorrhagic).
 - Gram staining and cytology.
 - Biochemistry (protein and sugar).
 - C/S (if the fluid is pyogenic).
 - If suspected tuberculosis: AFB staining, ADA of joint fluid may be done.
 - If gout is suspected: uric acid crystal (to be seen under polarizing light).
7. Others:
 - Blood for C/S (if septic arthritis).
 - If SLE is suspected: ANA, anti-dsDNA.
 - USG of affected joint.
 - In some case, arthroscopy and synovial biopsy.
 - CT scan or MRI of the joint.

READ THE FOLLOWING TOPICS IN RELATION TO ARTHRITIS

Q: What are the causes of acute monoarthritis?

A: As follows (remember the mnemonic: **GRASP-TH**):

- **G:** Gout.
- **RA:** Reactive arthritis.
- **S:** Septic arthritis (pyogenic).
- **P:** Pseudogout.
- **T:** Trauma, tuberculosis.
- **H:** Haemophilia (in early age).

N.B.: In children, septic arthritis and JIA are common causes. Others: haemophilic arthritis, leukaemia and osteomyelitis.

Q: What are the causes of polyarthritis?**A:** As follows:

1. Infective (bacterial, viral).
2. Inflammatory:
 - Rheumatic fever.
 - Rheumatoid arthritis and its variants.
 - Seronegative arthritis (ankylosing spondylitis, Reiter's syndrome, enteropathic arthritis, psoriatic arthritis).
 - JIA (<16 years).
 - Collagen disease (SLE, dermatomyositis, systemic sclerosis, polyarteritis nodosa).
3. Degenerative (osteoarthritis).
4. Metabolic (gout, pseudogout).
5. Neuropathic arthropathy (Charcot's joint).
6. Haematological (haemophilic arthritis, Henoch–Schönlein purpura).
7. Others: polymyalgia rheumatica, sarcoidosis, haemochromatosis, acromegaly, hypertrophic osteoarthropathy, Lyme disease.

Q: What is oligoarthritis and polyarthritis?**A:** As follows:

- When less than 5 joints or joint groups are involved, it is called oligoarthritis (pauciarticular arthritis)
- When 5 or more than 5 joints or joint groups are involved, it is called polyarthritis.

Q: What are the differences between mechanical and inflammatory arthritis?**A:** As follows:

Features	Mechanical Arthritis	Inflammatory Arthritis
1. Age	Any	Below 40 years
2. Onset	Acute	Insidious >3 months
3. Family history	Absent	Usually positive
4. Exercise	Worse	Improved
5. With rest	Better	Worse
6. Morning stiffness	Absent	Present
7. Sleep disturbance	Absent	Present
8. Neurological signs	May be present	Absent
9. Range of movement	Asymmetrical	Symmetrical
10. Straight leg raising (SLR)	Positive	Normal
11. Swelling and warm	Absent	Present
12. Maximum pain	After movement	After rest
13. Crepitus in joint	Coarse crepitus	Fine crepitus
14. ESR and CRP	Normal	High

JUVENILE IDIOPATHIC ARTHRITIS (JIA/JCA)

Instructions by the examiner:

- Examine the legs or knee joints (patient is usually a child or young adult).

Presentation of a Case: (Present as Described Previously in Knee Joint. If Other Joints such as Ankle or Foot Joints are Involved, Describe Accordingly).

Q: What are your **differential diagnoses**?

A: As follows:

- Juvenile Idiopathic Arthritis (JIA/JCA)
- Rheumatic fever (if any joint deformity is present, it is against rheumatic fever).
- Sero-negative arthritis (such as reactive arthritis, ankylosing spondylitis)
- SLE.
- Viral arthritis.
- Acute leukaemia.

Q: What **relevants** do you like to see?

A: As follows:

- I want to examine the other joints and also spine.
- For systemic onset JIA (Still's disease): Hepatosplenomegaly, lymphadenopathy, erythematous skin rash (present during fever called **Salmon rash**), pleurisy, pericarditis and eye (to see iritis).
- Detailed history to exclude other causes of arthritis in children.



Deformity in knee and joints of upper limbs



Deformity in elbow and small chin



Spindle-shaped PIP

Q: Could it be **rheumatic fever**?

A: Unlikely, because in rheumatic fever, there is no deformity of joints and wasting of muscles. Moreover, rheumatic fever is diagnosed by major and minor criteria (rheumatic fever licks the joints and kills the heart).

Q: Why wasting of muscles in JIA?

A: Disuse and release of cytokines (interleukin 1, 6 and TNF).

Q: What are the causes of acute arthritis in children?

A: As follows:

- Rheumatic fever.
- JIA.
- Infections (bacterial, viral).
- Acute leukaemia.
- Henoch–Schönlein purpura.
- Haemophilic arthritis.
- Reactive arthritis.
- Others: sickle cell disease, psoriatic arthritis, SLE, osteomyelitis, hypermobility syndrome.

Q: What investigations should be done in JIA?

A: As follows:

- CBC with ESR (leucocytosis in Still's disease, may be lymphocytosis, thrombocytosis and high ESR).
- CRP (high).
- ACPA (negative).
- RA test (usually negative, positive in 10% cases).
- ANA, Anti-ds DNA (if SLE is suspected).
- X-ray of the involved joint.
- Other investigations to exclude other diseases (according to history and physical findings).

READ THE FOLLOWING TOPICS IN RELATION TO JIA

Q: What is JIA?

A: It may be defined as 'arthritis before 16 years of age and persisting for more than 3 months'.

Q: What are the types of JIA?

A: As follows:

1. Systemic onset (**Still's disease**): 10 to 15% cases.
2. Oligoarthritis (pauciarticular): More common in females, usually asymmetrical large joint involvement. It is of 2 types:
 - Oligoarthritis (persistent): Common (50 to 60%), 4 or less joints are affected, mainly knee, ankles and wrists, in asymmetrical pattern. Common in girls, 3 years of age. Uveitis may occur. Relatively good prognosis.
 - Oligoarthritis (extended): Occurs in 25% cases, arthritis of many joints may develop after 6 months, can be very destructive.
3. Polyarticular JIA: Involvement of more than 4 joints, 30 to 40% cases of JIA. It is of 2 types.
 - RA positive (usually also ACPA positive): Affects girls older than 8 years. Small joints of hands, wrist, ankle, feet are involved, later larger joints are involved. Can be very destructive.
 - RA negative: Affects more in girls younger than 12 years, but may be in any age. Arthritis like RA positive type but cervical spine, temporo-mandibular joint and elbows may be involved. ANA may be positive with chronic uveitis.

4. Other types of juvenile arthritis:

- Enthesitis-related JIA (asymmetrical arthritis of lower limb joints and enthesitis, associated with HLA-B27 and there is risk of iritis. It is the childhood equivalent of adult ankylosing spondylitis but spinal involvement is rare).
- Psoriatic arthritis (similar to adult psoriatic arthritis, can be very destructive).
- Unclassified.



Deformity of knee joint



Swollen knee joint with wasting



Salmon rash

Q: What are the features of systemic onset JIA (Still's disease)?

A: It affects boys and girls equally up to 5 years of age. After this, girls are more affected. Adult onset Still's disease is rare. Features are:

- Arthritis: Involving knee, wrist and ankle. Other joints may be involved.
- High fever: Intermittent type, may be continuous.
- Skin rash: Macular or maculopapular, Salmon pink coloured (called **Salmon rash**), appears with fever and disappears when fever subsides.
- Extra-articular features: Hepato-splenomegaly and lymphadenopathy (common). May be pericardial effusion, pleural effusion, DIC.
- In chronic cases: Micrognathia (small mandible), fusion of cervical spine, retardation of growth may be present.
- Investigations: high ESR, CRP, neutrophilia and thrombocytosis. Autoantibodies are negative.

Q: How to treat JIA?

A: As follows:

1. General measures:
 - Explanation and reassurance to the parents, also to the patient.
 - Rest during pain and passive movement of the limb to prevent contracture.
 - To relieve pain: NSAID.
 - Physiotherapy.
2. In severe cases: Steroid, preferably alternate days. Pulse methylprednisolone may be given, followed by MTX (prolonged use of steroid cause early fusion of epiphysis resulting in short stature. 3 mg prednisolone daily may cause this effect).

3. Disease modifying drugs should be given in all cases:
 - Methotrexate, 5 mg weekly (increase the dose gradually).
 - Sulphasalazine, 30 to 50 mg/kg (effective in enthesitis related JIA).
 - Others: IV immunoglobulin, ciclosporin, cytotoxic drug (cyclophosphamide, chlorambucil, azathioprine) may be tried.
 - If MTX fails: anti-TNF may be given (helpful in all cases, except systemic onset type). Etanercept may be used.
4. Orthopaedic surgery, if needed.

N.B.: If aspirin is used for fever or arthritis associated with viral infection like influenza below 12 years of age, it may cause Reye's syndrome. So, it should be avoided.

BRIEF NOTES ON ADULT STILL'S DISEASE

Definition: It is a disease of unknown cause, characterized by high fever, seronegative arthritis, skin rash and polyserositis. Usually, it is diagnosed by exclusion of other diseases. Common in young adults, 16 to 35 years of age, rare after 60 years. Recurrent episode occurs in one-third cases.

Diagnostic criteria of Adult Still's disease: 5 or more criteria including 2 or more major with exclusion criteria.

Major criteria:

- Quotidian fever $>39^{\circ}\text{C}$, lasting 1 week or longer.
- Arthralgia or arthritis, lasting 2 weeks or longer (knee, wrist and ankle).
- Typical rash (Evanescant macular, maculopapular, Salmon coloured, non-pruritic, common in chest, abdomen).
- Leukocytosis $>10,000/\text{mm}^3$ with $>80\%$ polymorphonuclear cells (usually very high, may be $>40,000$).

Minor criteria:

- Sore throat.
- Recent development of significant lymphadenopathy (usually cervical, may be generalized).
- Hepatomegaly or splenomegaly.
- Abnormal liver function tests.
- ANA and RA are negative.

Exclusion criteria: Infection, malignancy, other rheumatic disease.

N.B.: High fever with chill and rigor, sweating is common. Initially, arthritis may be mild, later may be severe. Other features are abdominal pain, myalgia etc.

Investigations:

1. CBC (shows low haemoglobin, high ESR and leucocytosis).
2. CRP (usually high).
3. RA and ANF (negative).
4. Serum ferritin is very high ($>10,000$).
5. Fibrinogen level (high).
6. AST and ALT (high).

Treatment:

- For pain and fever: NSAID (high dose aspirin 1 gm 8 hourly). Other NSAIDs-indomethacin, ibuprofen may be helpful. NSAID may be effective in 50% cases.
- If no response: high dose prednisolone (60 to 100 mg/day). When fever subsides, dose is tapered slowly. Steroid is necessary in 50% cases.
- Other drugs: chloroquine, hydroxychloroquine, methotrexate, sulphasalazine, azathioprine, cyclophosphamide.
- In chronic or resistant case: TNF antagonists such as etanercept or interleukin-1 receptor antagonist such as anakinra or interleukin-6 receptor antagonist such as tocilizumab may be given.

SEPTIC ARTHRITIS

Instructions by the examiner:

- Examine the legs or knee joints.

Presentation of a Case: (Present the Case as Described in Knee Joint Arthritis).

Q: What are the **differential diagnoses**?

A: Described in monoarthritis in knee joint arthritis (mention the causes according to the age of the patient).

Q: What are the **causes** of septic arthritis?

A: As follows:

- Haematogenous spread from skin or other site of infection.
- Direct puncture or joint aspiration or trauma.

Q: What are the **risk factors** for septic arthritis?

A: As follows:

- Pre-existing joint disease (e.g., Rheumatoid Arthritis).
- Diabetes Mellitus.
- Immuno-compromised state.

Q: What are the **presentations** of septic arthritis?

A: As follows:

1. Features of joints:
 - Severe acute or subacute monoarthritis, may be polyarthritis (if there is septicaemia).
 - Joint is swollen, hot, red with severe pain and restricted movement.
2. Systemic features: High fever, malaise and weakness.



Septic arthritis (ankle joint)



Septic arthritis (hand)



Septic arthritis (knee joint)

Q: What investigations should be done in septic arthritis?**A:** As follows:

- CBC with ESR (shows leucocytosis).
- CRP (high).
- Blood C/S.
- X-ray of the joint involved.
- Joint fluid aspiration: to see the physical character (turbid or purulent), biochemistry (shows high protein, low sugar), cytology (shows high WBC $>5,000/\text{mm}^3$), Gram staining and C/S.

Q: How to treat septic arthritis?**A:** As follows:

- Complete rest.
- For pain: NSAID.
- Antibiotic: flucloxacillin (2 gm IV 6 hourly) for 2 to 3 weeks, then oral (9 to 10 weeks). If allergic to penicillin, erythromycin or clindamycin may be given.
- In high risk or severe case, cephalosporine (cefuroxime 1.5 g 3 times daily) may be added.
- In immunocompromised patients, flucloxacillin 1 to 2 gm IV, 6-hourly plus gentamicin may be given.
- Joint aspiration may be necessary. Occasionally, surgical drainage.
- Early regular passive movement.

Q: What are the causes of infective arthritis?**A:** As follows:

- Bacterial: Staph. aureus (causing native arthritis), Staph. epidermidis (prosthetic arthritis), Streptococcus, Pneumococcus, Meningococcus, H. influenzae.
- Viral: Parvovirus B19, rubella, HBV, HIV.
- Gonococcal arthritis: There is purulent arthritis (may be fleeting) associated with pustular skin lesion, tenosynovitis, urethral discharge and history of sexual exposure.
- Tubercular arthritis.
- Lyme disease.

Q: What is Lyme disease? How to diagnose and treat?**A:** It is a disease, caused by *Borrelia burgdorferi* by the bite of infected tick (Ixodes). **3 stages of disease:**

- Early localized disease: within a week of tick bite, there is fever, headache, macular skin rash (erythema migrans), lymphadenopathy. Most cases recover spontaneously at this stage.
- Early disseminated disease: occurs days to weeks after the appearance of erythema migrans. Some patients may develop widespread rash and after several weeks or months, few untreated cases may develop neurological complications such as meningitis, encephalitis, cranial neuritis (unilateral or bilateral facial nerve palsy), peripheral neuritis or radiculopathies. Cardiac involvement (conduction block, myocarditis), myalgia, arthritis may also occur.
- Late Lyme disease: rare, can cause chronic arthritis, encephalomyelitis, other neurological disorders and acrodermatitis chronica atrophicans.

Diagnosis: by detection of antibody titre—IgM in the 1st month, IgG in later months.

Treatment:

- For pain: NSAID.
- Amoxicillin or doxycycline is given in early stage.
- Late disease should be treated with IV ceftriaxone or benzyl penicillin for 2 to 4 weeks.

Q: What is Poncet's disease?

A: It is a type of tuberculous arthritis, characterized by acute, reactive symmetrical polyarthritis, that affects in patient with extra-pulmonary, either visceral or disseminated TB, associated with tenosynovitis and arthritis.

- Underlying lymph node TB is common.
- Usually not associated with pulmonary TB.
- Knee joint is commonly affected.
- No mycobacteria are found in the joints.
- Improves with anti TB therapy.

HAEMOPHILIC ARTHRITIS

Instructions by the examiner:

- Examine the legs or knee joints.

Presentation of a Case (Patient is a Child or Young):

Inspection:

- Both knee joints are swollen, erythematous and deformed, right one more than the left.
- Muscle wasting is present around both knee joints, more over the right knee.
- There are few ecchymosis of various sizes over the right thigh.

Palpation:

- Both knee joints are warm and tender.
- Patellar tap is positive.
- Movement is restricted.

My differential diagnoses are:

- Juvenile idiopathic arthritis (JIA).
- Rheumatic fever.
- Haemophilic arthritis (due to haemophilia A).
- Christmas disease with arthritis.
- Acute leukaemia.
- Septic arthritis.

Q: Ask one history to the patient.

A: I would like to ask any history of prolonged bleeding following any trauma, injury or tooth extraction.

Q: Can it be rheumatic fever?

A: Yes, diagnosed by major and minor criteria (see in the chapter rheumatic fever in cardiology).

Q: Which joints are commonly involved in haemophilic arthritis?

A: Commonly knee, elbow, ankle and hip joints are involved.

- In infants, hip joint is commonly involved.
- In older children, knee joint is commonly involved.



Haemophilic arthritis (knee joint)



Haemophilic arthritis (knee joint)

Q: What is the cause of joint deformity in haemophilia?

A: It is due to secondary osteoarthritis and wasting of muscles around the joint.

Q: What are the presentations of haemophilic arthritis?

A: Haemarthrosis occurs when plasma level of factor VIII:C is <1%. Arthritis may be spontaneous without trauma or may follow even minor trauma.

- Initially: tingling, abnormal sensation, stiffness and instability of the joint.
- Later on: the joint is red, hot, swollen and painful.

Progression of arthritis depends on repeated haemarthrosis, which leads to:

- Synovium hypertrophy.
- Fibrotic change in synovium.
- Destruction of cartilage with reduction of joint space.
- Subchondral cyst formation, bony erosion, marginal sclerosis, osteophyte formation and ankylosis of joint.

Q: What are the radiological features of haemophilic arthritis?

A: As follows:

- Initially, joint space is increased with widening of intercondylar notch in knee joint (indicates chronic haemorrhage).
- Later, reduction of joint space, periarticular osteopenia, marginal sclerosis, subchondral cyst formation, secondary osteoarthritis (with osteophyte) and ankylosis of joint.

Q: What are the causes of haemarthrosis?

A: As follows:

- Trauma.
- Haemophilia.
- Christmas disease.
- Von Willebrand disease.
- Sickle cell disease.
- Excess anticoagulant.
- Rarely, malignancy.

Q: How to treat haemophilic arthritis?

A: As follows:

- Complete rest, elevation of the affected limb and immobilization by splinting.
- Analgesic may be given (paracetamol or acetaminophen or codeine). Aspirin or other NSAIDs are avoided (as they interfere with platelet function and may cause excess bleeding).
- Factor VIII transfusion 20 to 30 IU/kg. Repeated after 12, 24 and 36 hours (higher dose is required, if treatment is delayed).
- Once acute stage is over, the patient should be mobilized, physiotherapy should be started (isometric exercise, followed by active movement, hydrotherapy).
- Arthrocentesis (aspiration from joint) is rarely necessary.

READ THE FOLLOWING TOPICS IN RELATION TO HAEMOPHILIA

Q: What is **haemophilia**?

A: It is an X-linked inherited recessive disorder due to deficiency of factor VIII (anti-haemophilic factor) or factor IX (Christmas factor), characterized by prolonged bleeding. Usually, female is the carrier and male is the sufferer. There is high rate of new mutations, in 30% no family history.

Q: What are the **types** of haemophilia A?

A: Normal factor VIII level is 50 to 150 IU/dL. According to severity, it is of 3 types:

- Mild: Factor VIII is >5 IU/dL (bleeding occurs following major injury or surgery).
- Moderate: Factor VIII is 1 to 5 IU/dL (bleeding occurs following minor injury or surgery).
- Severe: Factor VIII is <1 IU/dL (spontaneous bleeding into the joints, muscles).

Q: What is the **pedigree** of haemophilia?

A: As follows:

1. If father is affected:
 - All daughters are carriers.
 - All sons are normal.
2. If mother is carrier:
 - 50% daughters are carriers.
 - 50% sons are sufferers.

N.B.: Remember the following points:

- *In female carrier, 1 son is affected, 1 son is normal, 1 daughter is carrier and 1 daughter is normal.*
- *In a female carrier, factor VIII is $<50\%$ normal, because of randomized inactivation of one X-chromosome.*

Q: Can a **female** be the **sufferer** in haemophilia?

A: Yes, rarely a female can suffer, because of the following reasons:

- If her mother is a carrier and father is a sufferer of haemophilia.
- Turner's syndrome (45, XO).
- According to lyonization theory, there is randomized inactivation of one X chromosome in the developing foetus. Then the number of affected X chromosome may be predominant. Female may be affected, if normal X chromosome is disproportionately inactivated.

Q: How does a patient with haemophilia usually **present**?

A: Depends on whether factor VIII deficiency is mild, moderate or severe.

- Prolonged and persistent bleeding after trauma or injury, tooth extraction.
- Sometimes, spontaneous bleeding may occur in severe cases.
- Bleeding into the large joints and muscles (psoas and calf muscle) is also common.

Q: What is the common site of **muscular bleeding**?

A: Commonly in calf muscles and psoas.

Q: What happens if the patient has **bleeding into the psoas muscle**?

A: As follows:

- Severe pain in lower abdomen.
- Paraesthesia in thigh and weakness of quadriceps due to compression of femoral nerve.

Q: What **investigations** are done in haemophilia?

A: As follows:

- CBC with ESR, platelet (usually normal).
- Bleeding time (normal).
- Prothrombin time (normal).
- Clotting time (prolonged).
- APTT (prolonged).
- Factor VIII:C assay (deficient or absent).
- vWF (normal).
- Serum fibrinogen (normal).
- X-ray of involved joint (in haemophilic arthritis).

N.B.: APTT is prolonged, which is corrected by addition of normal plasma. If not corrected after the addition of normal plasma, more likely there is antibody formation or the presence of antiphospholipid antibody.

Q: Is **antenatal diagnosis** possible?

A: Yes. Antenatal diagnosis may be done by molecular analysis of foetal tissue obtained by chorionic villus biopsy at 11 to 12 weeks of pregnancy.

Q: How will you **manage haemophilia**?

A: As follows:

1. Management of bleeding episode:
 - Factor VIII concentrate by intravenous infusion, twice daily as its half-life is 12 hours and the blood level usually maintained for 3 to 5 days.
 - In minor bleeding: factor VIII level should be raised to 20 to 30 IU/dL. However, desmopressin 0.3 microgram/kg 12 hourly infusion over 20 minutes may be given, which raise factor VIII.
 - In severe bleeding: factor VIII level should be raised to at least 50 IU/dL. Treatment is continued for 1 week or more.
 - For major surgery, factor VIII level should be raised to 100 IU/dL preoperatively and maintained above 50 IU/dL until healing. Continuous infusion may be needed. Treatment to be continued for 7 to 10 days.
2. If factor VIII is not available, cryoprecipitate, fresh frozen plasma or fresh blood can be given.
3. To prevent recurrent bleeding into joints and subsequent joint damage, factor VIII infusions should be given regularly thrice a week starting from early childhood (around 2 years of age).
4. Synthetic vasopressin (desmopressin, an analogue of vasopressin) is given IV, subcutaneous or intranasally. It produces 3 to 5 fold rise in factor VIII:C and is very useful in patient with factor VIII >10 IU/dL. It prevents the complications associated with blood products. Also, useful for treating bleeding episodes in mild haemophilia and as prophylaxis before minor surgery. It is ineffective in severe haemophilia, also helpful in vWD, but not in Christmas disease.

Advice to the patient:

- Trauma should be avoided and precaution should be taken before tooth extraction and surgery.
- The patient should carry a special medical card in which details of the disease and its treatment must be recorded.

N.B.: Remember the following points:

- 1 unit/kg factor VIII will raise blood level by 2%. So, the dose of factor VIII is calculated as follows:
- $FVIII \text{ dose} = (\text{Desired factor VIII level} - FVIII \text{ baseline level}) \times \text{Body weight (kg)} \times 0.5 \text{ unit/kg.}$
- Previously, factor VIII was prepared from plasma. It is now prepared by recombinant DNA technology (so, there is less risk of transfusion transmitted infection, but more expensive).
- Half life of Factor VIII is 12 hours.

Q: What are the **complications** of haemophilia?**A:** As follows:

1. Due to repeated haemorrhage:
 - Arthropathy due to repeated bleeding in joint (e.g., knee, elbow).
 - Atrophy or wasting of muscles secondary to haematoma in muscle.
 - Mononeuropathy due to pressure by haematoma.
 - Death may occur due to intracerebral haemorrhage.
2. Due to therapy:
 - Infections: Hepatitis A, B, C, D. Also, HIV.
 - Factor VIII antibody (up to 30% patients with severe haemophilia, usually after few doses of factor VIII infusion).

N.B.: Remember the following points:

- Risk of viral transmission is eliminated because of prior screening of donors.
- Infectious agents that can cause Creutzfeldt–Jakob disease may be transmitted by blood and blood products.
- All patients should receive vaccination for HAV and HBV.
- Use of recombinant factor VIII effectively eliminate transfusion transmitted infection.

Q: What are the **causes of death**?**A:** As follows:

- Bleeding, mainly intracerebral.
- HIV related.
- Hepatitis due to HBV and HCV.

Q: If factor VIII antibody develops, how can it be suspected and treated?

A: It is suspected if no response to factor VIII in therapeutic dose. APTT is prolonged. In normal haemophilia, APTT is corrected by addition of normal plasma in 1:1 ratio. But if factor VIII antibody develops, APTT is not corrected with normal plasma in this ratio. This case is very difficult to treat. Following options are available:

- High dose and frequent infusion of factor VIII may be given.
- Changing the species such as porcine factor VIII may be used.
- Factor IX may be used. It helps bypassing the inhibitors.
- Recombinant factor VIIa helps bypassing the inhibitors.
- Factor eight inhibitor bypassing activity (FEIBA, an activated concentrate of factors II, IX and X), or, prothrombin complex concentrate (PCC), which contains factor VII, IX and X may be used.
- Sometimes, immunosuppressive therapy such as steroid, azathioprine or cytotoxic drugs may be given.
- To eradicate inhibitory antibody: immune tolerance induction (ITI).
- Recently, anti-CD20 monoclonal antibody (rituximab) as co-adjuvant is promising.

Christmas Disease: It is also called haemophilia B, due to deficiency of factor IX. Features are like haemophilia A. It is treated with factor IX concentrate, half-life is 24 hours. Prophylaxis is given twice a week. Desmopressin is ineffective.

REITER'S SYNDROME (OR, REACTIVE ARTHRITIS)

Instructions by the examiner:

- Examine the legs or knee joints or lower limbs.

Presentation of a Case: (Present as Described in Knee Joint, the Patient is Usually Young Adult).

Q: What **history** do you like to take from the patient?

A: History of urethritis, diarrhoea or dysentery (due to *Shigella*, *Campylobacter*, *Yersinia*) and sexual exposure (*Chlamydia*).

Q: What **else** do you want to examine?

A: As follows:

- Eyes (to see conjunctivitis, usually bilateral, may be iritis in 10%).
- Back (to see evidence of sacroiliitis).
- Foot (to see heel pain, Achilles tendinitis and plantar fasciitis).
- Circinate balanitis and keratoderma blennorrhagica (in palm, sole and toes).



Circinate balanitis (glans penis)



Keratoderma blennorrhagica



Keratoderma blennorrhagica

Q: What is the **triad** of Reiter's syndrome?

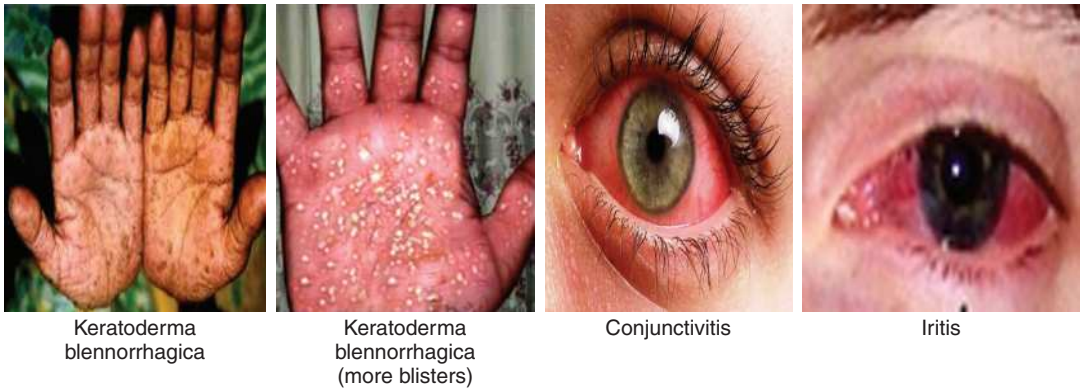
A: Triad is:

- Arthritis (seronegative).
- Conjunctivitis or Uveitis.
- Urethritis (non specific).

Q: What is **Reiter's syndrome** and **reactive arthritis**?

A: As follows:

- Reiter's syndrome is a seronegative arthritis characterized by triad of arthritis, conjunctivitis and urethritis.
- Reactive arthritis means when only arthritis follows after an attack of diarrhoea or dysentery or sexual exposure (pathology in one site, but affecting the joints), no conjunctivitis. It is actually a variety of Reiter's syndrome. Organisms are *Salmonella*, *Shigella*, *Campylobacter*, *Chlamydia* and *Yersinia*.



Q: How does a patient with Reiter's syndrome usually present?

A: Reiter's syndrome is common in males (M:F = 15:1), 16 to 35 years. Male with HLA B27 has 20% risk of suffering the disease after *Shigella* dysentery.

1. History of diarrhoea, dysentery or sexual exposure. After 1 to 3 weeks, asymmetrical oligoarthritis involving the bigger joints (knee and ankle), conjunctivitis and urethritis.
2. Extra articular features:
 - Conjunctivitis and iritis.
 - Achilles tendinitis and plantar fasciitis.
 - Circinate balanitis.
 - Skin rash (macular, vesicular or pustular).
 - Keratoderma blennorrhagica (in palm, sole or toes).
 - Nail dystrophy and buccal erosion.
 - Others: pericarditis, aortic regurgitation, conduction defect, pleurisy, peripheral neuropathy, meningoencephalitis.

Q: What investigations should be done in Reiter's syndrome?

A: As follows:

- CBC with ESR.
- Urine RME (shows pus cells, sterile on routine culture, called sterile pyuria).
- CRP (high).
- RA test and ANA (negative).
- X-ray of the joints involved and SI joint (may show ankylosing spondylitis in advanced stage).
- If joint effusion is present: aspiration of fluid and analysis (complement is high in synovial fluid, may contain giant macrophages, called Reiter's cell).
- HLA-B27 positive in 70% cases (in affected persons).
- Serology and cultures (blood, urine, stool, cervix, urethra), particularly for Chlamydia.

Q: What is keratoderma blennorrhagica?

A: It is a type of skin lesion, characterized by vesiculo-papules with desquamated margin, which coalesces to form crusty plaques. Usually found in palm and sole, also in scrotum, scalp and trunk. It may disappear and recur also. Nail dystrophy and subungual hyperkeratosis may occur. It is confused with pustular psoriasis. Treated with methotrexate or azathioprine.

Q: How to treat Reiter's syndrome?**A:** As follows:

- For pain: Rest and NSAID. Sometimes in severe pain, local steroid injection (methylprednisolone or triamcinolone).
- Antibiotic (tetracycline or erythromycin for non-gonococcal urethritis).
- In severe cases: systemic steroid may be given.
- Usually, single attack, which settles. In some cases, there may be recurrent and remitting arthritis. In such case, disease modifying drugs, such as sulphasalazine or methotrexate or azathioprine may be given.
- Anti-TNF α therapy may be helpful in some severe cases.
- Physiotherapy.

Q: What are the differences between gonococcal arthritis and Reiter's syndrome?**A:** As follows:

Features	Gonococcal Arthritis	Reiter's Syndrome
1. Involvement of joints	Mainly of upper and lower extremities	Mainly lower extremity
2. Vesicular lesion	Common	Uncommon
3. Backache (ankylosing spondylitis)	Unusual	Common
4. Organism	<i>Gonococcus</i> isolated from smear	No definite organism found

Q. What are the indications of DMARD in Reiter's syndrome?**A.** As follows:

- Severe and persistent symptoms.
- Recurrent arthritis.
- Severe keratoderma blennorrhagica.

Q. What are the indications of steroid in Reiter's syndrome?**A.** Severe symptoms not responding to NSAID and severe uveitis (local or systemic).

PSORIATIC ARTHROPATHY

Instructions by the examiner:

- Examine the lower limbs or knee joints. Or, examine the hands. What else do you like to examine?

Presentation of a Case (Suppose Lower Limbs or Knee): Case No. 1

- Present the case as described in knee joint arthritis.

My differentials are: Mention as described in knee joint arthritis.

Q: What else do you want to examine?

A: I want to examine the skin to see psoriatic patch and nail changes.

Q: What is your diagnosis?

A: Because of presence of psoriatic patch, my diagnosis is psoriatic arthritis.

Presentation of a Case (Hand): Case No. 2

- There is swelling with gross deformity of right (or left), second and third DIP joint and first PIP joint.
- There is also (may be) deformity of MCP (mention which one). Arthropathy is asymmetrical.
- In nails: pitting, thickening of nail plate, hyperkeratosis and onycholysis are seen.
- There is psoriatic patch at the dorsum of right (or left) hand.

My diagnosis is **Psoriatic arthritis**.



Knee joint arthritis with psoriatic patch



Arthritis in hand with psoriatic patch



Typical skin lesion in psoriasis



Psoriatic arthritis (DIP) with patch and nail lesion

Q: What are the sites of psoriatic patch?

A: Wrist, elbow, scalp, hairline, back of ear, natal cleft, around umbilicus, shin, knee, extensor surfaces of limbs, scrotum.

Q: Why **not** this is a case of rheumatoid arthritis?

A: Because in rheumatoid arthritis:

- PIP joints are involved. No involvement of DIP.
- Arthritis is usually bilateral and symmetrical.
- Skin lesions and nail changes are against rheumatoid arthritis.



Onycholysis



Subungual hyperkeratosis



Nails pitting



Ridging in nail

Q: What are the **types of arthritis** in psoriasis?

A: 5 types:

- Asymmetrical inflammatory oligoarthritis (of hands and foot): 40%.
- Symmetrical seronegative polyarthritis (like rheumatoid): 25% (no rheumatoid nodule and involvement of PIP, DIP, MCP joints and nail changes help to diagnose. 50% of cases develop arthritis mutilans).
- Sacroiliitis or spondylitis: 15%. More in males, psoriatic lesion before arthritis, nail changes are usually present.
- Predominant DIP joint arthritis: 15% (typical), nail dystrophy is invariable.
- Arthritis mutilans: 5%.

Q: What are the **nail changes** in psoriasis?

A: Nail change is present in 85% cases of psoriasis. Rarely, nail changes may precede the onset of skin disease. 5 types of nail changes are found:

- Nail pitting.
- Onycholysis (distal separation of nail plate).
- Subungual hyperkeratosis.
- Horizontal ridging and thickening of nail.
- Yellow brown discoloration.

Q: What are the other diseases causing **nail change**?

A: As follows:

- Fungal infection.
- Reiter's syndrome.

Q: What are the diseases affecting **DIP joint**?

A: As follows:

- Psoriatic arthritis.
- Gout.
- Osteoarthritis.

Q: What are the causes of arthritis mutilans?**A:** As follows:

- Rheumatoid arthritis.
- Psoriatic arthritis.
- Juvenile idiopathic arthritis.

Q: What investigations should be done in psoriatic arthritis?**A:** Diagnosis is clinical. For exclusion of other diseases, following tests are done:

1. CBC with ESR (ESR may be high).
2. CRP (high).
3. RA and ANA (both are negative).
4. Serum uric acid (may be high), can cause secondary gout.
5. Radiology: X-ray of the joint involved (hand, foot and sacroiliac joint). May be normal. In advance stage, may show:
 - X-ray hand shows destruction of DIP joint with deformity, punched out lytic lesion, pencil in cup appearance (narrow distal end of proximal bone fits into the splayed out proximal end of distal bone). Extensive bone resorption results in '**opera glass hand**' (one bone enters into its neighbouring bone like a telescope, giving rise to this appearance).
 - X-ray of sacroiliac joint (may show ankylosing spondylitis).

Q: How to treat psoriatic arthritis?**A:** As follows:

1. Treatment of psoriasis: General measures, local therapy and systemic therapy (for details see in chapter **Dermatology**).
2. Treatment of arthritis:
 - For pain: NSAID (however, some NSAIDs may aggravate psoriasis).
 - In persistent and progressive cases: Sulphasalazine, methotrexate or azathioprine (these drugs will help in both skin lesion and arthritis). Cyclosporine may be used.
 - A retinoid, acitretin 20 mg daily is effective in both arthritis and skin lesion (avoid in young female as it is teratogenic).
 - Prednisolone may be needed (sometimes steroid is given intra-articularly).
 - PUVA is mainly for skin lesion. Sometimes helpful in arthritis when synchronous skin lesion and arthritis are present.
 - Biological agents: when all other drugs fail, monoclonal antibody may be given. It produces dramatic response (e.g., infliximab, etanercept or adalimumab may be given. Rituximab has no role in psoriatic arthritis).

N.B.: Remember the following points:

- 5 to 8% of psoriasis patients develop arthritis.
- Arthritis occurs in 20% cases before the onset of psoriasis. Arthritis is present with current or previous psoriasis in 70% cases. In 5% cases, synchronous onset of skin lesion and arthritis may occur.
- No skin lesion in 5% cases.
- Age: Third or fourth decade (25 to 40 years).
- Equally affects both males and females (but ankylosing spondylitis is twice more in males than in females).
- 50% patients with ankylosing spondylitis are HLA-B27 positive.
- Spontaneous remission of arthritis may occur.

Q: What **drugs** should be avoided in psoriatic arthritis?

A: Avoid the following drugs (which may aggravate psoriatic skin lesion, even may cause exfoliative lesion):

- Chloroquine.
- Hydroxychloroquine.
- Lithium.
- Beta-blocker.
- ACE inhibitor.
- Alcohol.

Q: Name some **drugs** that are effective both in psoriasis and arthritis.

A: Methotrexate, sulphasalazine, cyclosporine, azathioprine and biological agents.

Q: What are the **common** complications of anti-TNF- α therapy?

A: As follows:

- Flare of tuberculosis.
- Haematological malignancy (lymphoma).
- Worsening of heart failure.
- Blood dyscrasia such as anaemia, thrombocytopenia, leucopenia, aplastic anaemia.

Q: What are the **contraindications** of anti-TNF α therapy?

A: As follows:

- Active tuberculosis (2 months anti-TB therapy should be given before starting anti-TNF α therapy).
- Latent tuberculosis.
- Active bacterial infection.
- CCF.
- Septic arthritis in previous 1 year.
- Demyelinating disease.
- Pregnancy and breast feeding.

Q: What are the **new drugs** for psoriasis?

A: As follows:

- Anti-TNF- α agents golimumab and anti-IL-12/23 inhibitor ustekinumab, are highly effective and safe for severe skin and joint disease. Can be used when methotrexate fails.
- Brodalumab (an anti-IL-17 receptor), ixekizumab (anti-IL-17) and secukinumab (anti-IL-17A).
- Apremilast, a PDE4 inhibitor may be given orally.

ANKYLOSING SPONDYLITIS

Instructions by the examiner:

- Examine the back and relevant parts.
- Look at the patient and examine (patient may be standing or lying).

Proceed as follows (patient should be examined in lying and in standing position):

During lying:

- See SLR (ask the patient to raise the leg straight above. The patient may complain of pain on the affected side, which indicates root pressure due to disc prolapse).
- Abdomen (appears protruded).
- Examine for evidence of sacroiliitis (compressing iliac bones).
- Assess the movement of hip joint.
- See chest expansion and examine lungs for apical fibrosis.
- Examine heart for aortic regurgitation (AR).
- Examine the eyes (for iritis).
- Examine the foot for Achilles tendinitis and plantar fasciitis.

Now, ask the patient to stand up and perform the following points:

- Observe whether there is fixed thoracic kyphosis, loss of lumbar lordosis and compensatory hyperextension of neck.
- Ask the patient to look up (patient is unable to do so).
- Ask the patient to turn either side (whole body turns, while the patient is attempting to do so).
- Ask the patient to stand along the side of wall with heel and back against the wall, now measure occiput to wall distance. Gap indicates limitation of thoracic and cervical spine. Patient is unable to make contact the body against the wall.
- See the range of movement of spine by flexion, extension and lateral bending of the body (see any restriction).
- Perform Schober's test as follows:
 - Mark two points 10 cm above and 5 cm below a line joining the dimple of Venus on the sacral promontory (the line passes along L₅ and the dimple indicates the site of posterior superior iliac spine).
 - Ask the patient to bend forward as far as possible.
 - Now measure the distance between upper and lower markings.

Normally, it increases by >5 cm below 50 years of age. If <5 cm, it indicates limitation of mobility of spine.

Modified Schober's test: Only upper marking is taken, as the lower part is fixed. It is called modified Schober's test.

Q: Ask some questions to the patient?

A: Low back pain with morning stiffness, any skin lesion (indicates psoriatic arthritis) and history of frequent loose motion or bloody diarrhoea (indicates inflammatory bowel disease).

Presentation of a Case:

- Abdomen is protruded. SLR is positive.
- There is loss of lumbar lordosis, thoracic kyphosis and compensatory hyperextension of neck (in advanced stage, **question mark** or stooped posture).
- The patient is unable to look up and unable to turn to any side without movement of whole body.
- He is also unable to make contact between the occiput and the wall when standing with heel and back against the wall.
- There is restricted movement of spine in all directions (forward, lateral and backward bending).
- Sacroiliitis, Achilles tendinitis and plantar fasciitis are present.
- Right knee joint is mildly tender and swollen with slight reduction of movement.
- Schober's test is positive.

My diagnosis is **Ankylosing spondylitis**.

Q: What are your **differential** diagnoses?

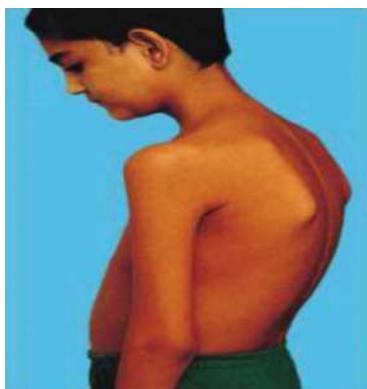
A: As follows:

- Enteropathic arthritis (Crohn's disease and ulcerative colitis).
- Psoriatic arthritis.
- Juvenile chronic arthritis (if the patient is <16 years old).

Q: What **else** do you want to see in ankylosing spondylitis?

A: I want to see extra-articular features:

- Eye (to see iritis).
- Heart (AR).
- Chest and lungs (restricted movement of chest, apical fibrosis, pulmonary hypertension and cor pulmonale).
- Foot (Achilles tendinitis and plantar fasciitis).



Juvenile ankylosing spondylitis



Protruded abdomen, thoracic kyphosis, lumbar lordosis



Stooping forward posture

Q: What are the other **causes** of sacroiliitis?

A: Any cause of spondylo-arthropathy.

Q: How to **differentiate** aortic regurgitations of rheumatic heart disease and of ankylosing spondylitis?

A: From **history** and **echocardiogram**:

- In rheumatic fever: echocardiogram shows involvement of valve cusps (there is shortening, thickening and fusion).
- In ankylosing spondylitis: echocardiogram shows involvement of aorta or aortic root dilatation due to aortitis.

Q: What is **spondyloarthropathy** or **spondarthritis**?

A: It is a group of inflammatory arthritis characterized by:

1. Seronegative rheumatoid factor (RA test is negative).
2. Sacroiliitis and inflammatory spondylitis.
3. Asymmetrical inflammatory oligoarthritis (lower > upper limbs, bigger joints are usually involved).
4. Inflammatory enthesitis.
5. Absence of nodules and other extra-articular features of rheumatoid arthritis.
6. Typical overlapping extra-articular features:
 - Mucosal inflammation (such as conjunctivitis, buccal ulceration, urethritis, prostatitis, bowel ulceration).
 - Pustular skin lesions and nail dystrophy.
 - Anterior uveitis.
 - Aortic root fibrosis (causes AR, conduction defects).
 - Erythema nodosum.
7. Familial association (high in HLA-B27).

Q: What are the **diseases** in spondyloarthropathy?

A: As follows:

- Ankylosing spondylitis.
- Reiter's syndrome or reactive arthritis.
- Enteropathic arthritis (Crohn's disease and ulcerative colitis).
- Psoriatic arthritis.

Q: What are the **types** of ankylosing spondylitis?

A: 2 types:

- Primary: Without other association.
- Secondary: When associated with other seronegative arthritis (such as ankylosing spondylitis, Reiter's syndrome or reactive arthritis, enteropathic arthritis).

Q: What is **enthesopathy**?

A: Inflammation at the ligamentous attachment with erosion of adjacent bone. Healing of such lesion at the junction of intervertebral disc and vertebral bodies causes new bone formation, called syndesmophyte (**hallmark** of ankylosing spondylitis).

READ THE FOLLOWING TOPICS IN RELATION TO ANKYLOSING SPONDYLITIS

Q: What is **ankylosing spondylitis**? What are the usual **presentations**?

A: It is a chronic inflammatory sero-negative spondyloarthritis characterized by progressive stiffening and fusion of axial skeleton. Age is second and third decade, M:F = 3:1. The patient usually presents with low back pain with morning stiffness, worse in the morning and with inactivity, the pain improves after exercise.

Q: Is there any **peripheral arthritis** in ankylosing spondylitis?

A: May occur in juvenile onset disease, also in 20 to 30% of adult cases. Hip and knee joints are commonly affected.

Q: What is the cause of **chest pain** in ankylosing spondylitis?

A: Chest pain is due to costo-chondral junction involvement.

Q: What is the **nature of arthritis** in ankylosing spondylitis?

A: Inflammatory.

Q: What are the **extra-articular manifestations** of ankylosing spondylitis?

A: As follows:

1. Eyes: Uveitis (iritis) 25%, conjunctivitis 20% (the patient may present with painful red eye and photophobia).
2. Heart:
 - Aortic regurgitation (4%, due to aortitis), mitral regurgitation.
 - Conduction defect (1st degree block, left bundle branch block), atrioventricular block, pericarditis.
3. Chest and lungs:
 - Chest pain (pleuritic) and reduced chest expansion (due to costo-vertebral joint involvement).
 - Apical pulmonary fibrosis, cavitation and aspergilloma may occur.
 - Pulmonary hypertension and cor pulmonale.
4. Prostatitis (80%), usually asymptomatic.
5. Neurological: Cauda equina syndrome (weakness of lower limbs, loss of sphincter and rectal control, saddle sensory loss).
6. Others: plantar fasciitis, Achille tendinitis, amyloidosis and osteoporosis.

Q: What are the **diagnostic criteria** for AS?

A: 3 of the following 4 criteria in adults <50 years with chronic back pain indicates AS:

- Morning stiffness >30 minutes.
- Improvement of back pain with exercise but not rest.
- Awakening because of back pain during second half of night only.
- Alternating buttock pain.

Alternately, Modified New York Criteria (1984) is used:

- Low back pain at least 3 months duration, relieved by exercise.
- Limitation of lumbar spine movement in at least 2 planes.
- Decreased chest expansion less than normal.
- Bilateral sacroiliitis grade 2 to 4.
- Unilateral sacroiliitis grade 3 to 4.

Definite AS: Sacroiliitis with any clinical criteria.

Q: What investigations should be done in ankylosing spondylitis?

A: As follows:

- X-ray of SI joints and spine (lumbosacral, dorsal and cervical).
- MRI of lumbosacral spine may be done in some cases (more sensitive than X-ray).
- CBC (ESR may be high).
- CRP (may be high).
- Rheumatoid factor (negative).
- HLA-B27 (positive in 90% cases).
- Others according to cause (barium enema and follow through for inflammatory bowel disease, colonoscopy).

N.B. HLA-B27 is neither necessary nor sufficient for diagnosis of AS. Positive HLA-B27 increases the probability of AS.

X-ray shows:

- Sacroiliitis: Starts in the lower parts of SI joints with irregularity and loss of cortical margins, widening of joint space and subsequently sclerosis, narrowing and fusion.
- In thoracolumbar spine: Squaring of vertebrae due to erosion. Syndesmophytes formation with bridging results in **bamboo spine appearance**. There may be ossification of anterior longitudinal ligament or interspinous ligament and facet joint fusion.

Radiographically, ankylosing spondylitis may be confused with alkaptonuria, DISH, lumbar spondylosis and osteitis condensans ilii. Features are as follows:

- In Alkaptonuria: calcification looks like AS. But there is calcification of intervertebral disc in alkaptonuria, never in AS.
- DISH (Diffuse idiopathic skeletal hyperostosis): Florid new bone formation along the anterolateral parts of at least four contiguous vertebral bodies. Calcification gives the appearance of **flowing wax** on the anterior body of vertebrae. Sacroiliac and apophyseal joints are normal in DISH. Common in middle aged and elderly, usually asymptomatic.
- In lumbar spondylosis: there is disc space narrowing and marginal sclerosis.
- In osteitis condensans ilii: there is sclerosis on the iliac site of sacroiliac joints, confuses with sacroiliitis. It is a post-partum radiographic finding.

Q: What are the **differences** between syndesmophyte and osteophyte?

A: As follows:

Syndesmophyte	Osteophyte
1. Secondary to inflammatory disease	Degenerative
2. It grows longitudinally (above or below) causing bridging of adjacent vertebra	It grows horizontally outwards
3. Due to endochondral calcification of annulus fibrosus	New bone at the corners of vertebra
4. It is the hallmark of ankylosing spondylitis	It is the hallmark of osteoarthritis

Q: What is the **natural history** of ankylosing spondylitis?

A: Up to 40% may develop severe spinal restriction, 20% may have significant disability. Early peripheral joint disease, especially hip joint involvement indicates poor prognosis.

Q: How would you perform **genetic counselling** with this patient?

A: If the patient is HLA-B27 positive, there is 30% chance for the siblings to develop ankylosing spondylitis.

Q: How to **treat** ankylosing spondylitis?

A: As follows:

- General measures:
 - Patient's counselling and education.
 - Exercise is the mainstay. The patient must remain active. Swimming is the best exercise.
 - Prolong sitting or inactivity should be avoided.
 - Physiotherapy.
 - Occupational therapy.
- Drug treatment:
 - NSAID to relieve pain.
 - DMARD: sulphasalazine or MTX should be given, helpful in peripheral arthritis, but has less effect on axial disease.
 - If persistent active inflammation: anti-TNF α (etanercept, adalimumab, infliximab) may be given.
 - Local steroid injection for persistent plantar fasciitis, other enthesopathies and peripheral arthritis.
 - Oral steroid may be needed for acute uveitis.
 - Other drugs: Thalidomide, pamidronate (may be used in resistant cases).
- Orthopaedic measures: for severe hip, knee or shoulder restriction.

Q: What is the **prognosis**?

A: With treatment, prognosis is better with minimum disability unless hip joints are involved. 80% patients remain active.

N.B.: Remember the following points:

- In women, disease is usually mild, peripheral arthritis is more, spinal arthritis is less.
- If occurs in early age, it may be severe with worse prognosis.
- Hip joint involvement is more in early age.
- Radiotherapy was given previously, but not used nowadays, because of increased incidence of leukaemia (AML).

DERMATOMYOSITIS OR POLYMYOSITIS

Instruction by the examiner:

- Look at the patient or face. What are your findings?
- Examine the hands and relevant parts of this patient.

In the **face**, see the following points:

- Skin rash (macular, maculopapular, scaly, erythematous) over the cheeks and forehead. There may be butterfly rash and erythema resembling sunburn.
- Heliotrope rash around the eyelid (commonly in upper eyelid).
- Periorbital oedema.
- Puffy face.
- Telangiectasia.
- Erythematous rash may be present on the neck and upper chest (V shaped, called **V** sign) or on shoulders (Shawl's sign).

In the **hands**, see the following points:

- Skin rash (macular, maculopapular, scaly, erythematous) on the dorsum of hands (usually spares the phalanges, unlike SLE that involves the phalanges, but spares the knuckles).
- Finger shows periungual erythema, dilated nail fold capillary (telangiectasia), ragged cuticles, haemorrhage.
- Gottron's sign (see below).
- Joint changes (swelling, tenderness or contracture).

For **relevant parts**, see the following points:

- Skin rash in other parts of the body.
- Look for signs of proximal myopathy (both in upper and lower limbs).
- Tenderness of muscles (present in 50% cases of polymyositis).

Presentation of Case No. 1 (by Looking at the Face):

- In the face: erythematous, maculopapular, scaly rash over the cheeks, bridge of the nose and forehead.
- There is heliotrope rash in upper eyelids of both eyes and periorbital oedema.

My diagnosis is **Dermatomyositis**.

Q: What else do you like to see?

A: I want to see skin lesion in other parts of the body, proximal myopathy and joints. Also, I want to exclude other primary causes, especially malignancy (such as bronchial carcinoma).



Face in dermatomyositis



Heliotrope rash in childhood dermatomyositis



Heliotrope rash and butterfly rash



Dermatomyositis

Q: What are the differential diagnoses?

A: As follows:

- Drug rash.
- SLE (or discoid lupus erythematosus, DLE).
- Mixed connective tissue disease (MCTD).
- Systemic sclerosis.
- Sarcoidosis.
- Acne rosacea.
- Lepromatous leprosy.

Presentation of Case No. 2 (Hand):

- There are multiple maculopapular, scaly, erythematous rash on the dorsum of both hands. Also, rashes with flat topped macules over the knuckles (Gottron's sign) are present.
- In the fingers: periungual erythema, ragged cuticles, haemorrhage and telangiectasia (dilated nail fold capillary).
- Joints are swollen, tender with flexion deformity involving with some fingers.

My diagnosis is **Dermatomyositis**.



Gottron's sign



Skin rash in dermatomyositis (body)



Dermatomyositis (contracture)

Q: What is polymyositis or dermatomyositis?

A: Polymyositis is the non-suppurative, non-infective inflammation of skeletal muscle characterized by necrosis, fibrosis and regeneration of muscles. When associated with **skin rash**, it is called dermatomyositis.

Q: What are the types of dermatomyositis/polymyositis?

A: 5 types:

1. Adult polymyositis.
2. Adult dermatomyositis.
3. Dermatomyositis or polymyositis associated with malignancies.
4. Childhood dermatomyositis or polymyositis associated with vasculitis.
5. Dermatomyositis or polymyositis associated with collagen vascular disease.

Q: What are the causes of dermatomyositis?

A: Actual cause unknown. Probable factors are:

- Autoimmune mechanism (due to the presence of anti-Jo-1 antibody and lymphocyte infiltration in muscle).
- Viral (coxsackie B, rubella and influenza have been suggested).
- Associated with malignancy (commonly bronchial carcinoma in male, ovarian carcinoma in female).
- Dermatomyositis can precede any malignancy of lungs, ovary, breast, stomach.
- Drugs causing polymyositis such as penicillamine and zidovudine.

Q: If the patient is elderly, what disease should be excluded?

A: Malignancy (bronchial carcinoma, also carcinoma of breast, GIT, ovary).

Q: What are the presentations of dermatomyositis?

A: Common in female, F:M = 2:1, peak incidence is in 50 to 60 years.

- Muscular weakness, mainly involving the proximal muscles (shoulder and pelvic girdle).
- Skin rash: typically affects upper eye lids with erythema called 'heliotrope rash'. Flat, red rash on face and upper trunk, erythematous rash of knuckles with raised violaceous scaly eruption (Gottron's sign). Erythematous rash also may occur in knee, elbow, malleoli, neck and anterior chest (often a V sign) or back and shoulder (shawl's sign).
- Pharyngeal, laryngeal and respiratory muscles involvement may cause dysphagia, dysphonia and respiratory failure.
- Others: Arthralgia, arthritis, myalgia and Raynaud's phenomenon.

N.B.: Remember the following points:

- *In some patients, only skin rash may be present without muscle involvement called dermatomyositis sine myositis.*
- *Ocular involvement is rare.*
- *Malignancy is more in dermatomyositis, less in polymyositis.*
- *The patient may present with acute renal failure due to myoglobinuria secondary to rhabdomyolysis.*

Q: What is the pathognomonic sign in dermatomyositis?

A: Heliotrope rash.

Q: What is heliotrope rash?

A: It is a violaceous, purple or lilac coloured rash, present usually over the eyelids. It may also be present on the cheeks, nasal bridge and knuckles. Presence of heliotrope rash is highly suggestive of dermatomyositis. It is derived from the name of a shrub *Heliotropium*, which has fragmented, purple flowers. It is common in childhood dermatomyositis.

Q: If the patient is elderly, what do you think is the underlying cause?

A: May be associated with neoplasm (commonly bronchial carcinoma, also carcinoma of the breast, GIT and ovary).

Q: What is Gottron's sign?

A: It is scaly, purple-red, raised, flat-topped and vasculitic patches over the extensor surface of joints and knuckles of hands. It may be found on the elbow and knee.

Q: What other skin lesion may resemble Gottron's papule?

A: SLE, psoriasis, lichen planus.

Q: What investigations should be done in dermatomyositis?

A: As follows:

1. CBC with ESR (ESR is high, but may be normal even in active disease).
2. Muscle enzymes:
 - CPK is very high (the most sensitive test).
 - Other enzymes: serum aldolase, SGOT, SGPT and LDH (may be high).
3. Electromyography: abnormal almost in every case, normal in 10%.
4. Muscle biopsy shows the following findings:
 - Necrosis, swelling, vacuolation, disruption and fragmentation of muscles.
 - Infiltration of lymphocyte, plasma cells, eosinophils and macrophages.
 - Fibrosis and perivascular inflammatory cells infiltration and thickening of vessel wall.
5. Other tests:
 - To exclude malignancy (chest x-ray, USG, CT scan, MRI, PET scan, mammogram, gastrointestinal tract imaging).
 - Other x-rays (limbs or hands) to see soft tissue calcification. It is common in childhood dermatomyositis.
 - RA test and ANA (positive in 50% cases).
 - Anti-Jo-1 antibody. Positive in 30% in dermatomyositis and 50% in polymyositis (if anti-Jo-1 antibody is present, respiratory muscles involvement may occur).
 - MRI of muscles, to detect abnormal muscles (helpful to take biopsy).
 - Urine for myoglobin in acute cases.

Measurement of CPK is important for the following reasons:

- Very high in dermatomyositis.
- Indicates active disease.
- To see therapeutic response (reduces after therapy).

Occasionally, CPK may be **normal** in dermatomyositis:

- If dermatomyositis is associated with internal malignancy.
- Due to longstanding disease with atrophy of muscles.
- Due to the presence of inhibitors in blood.

Q: What are the causes of high CPK?**A:** As follows:

- Exercise.
- Intramuscular injection.
- Muscle trauma or road traffic accident.
- Convulsion.
- Alcoholism.
- Dermatomyositis or polymyositis.
- Acute myocardial infarction (CPK-MB is high).
- Myopathy.
- Rhabdomyolysis.
- Chronic liver disease.
- Drugs: statins, busulfan, narcotics, colchicine and chloroquine.

Q: What are the isoenzymes of CPK?**A:** 3 types:

- MM (mainly in skeletal muscle).
- MB (mainly in cardiac muscle).
- BB (in brain).

Q: What are the EMG findings in dermatomyositis?**A:** As follows:

- Spontaneous fibrillation (at rest).
- Small amplitude, short duration and polyphasic action potential (after voluntary activity).
- Salvos of repetitive potential on mechanical stimulation of the nerve.

Diagnostic criteria of dermatomyositis:

4 criterions:

- Typical clinical history.
- Increased muscle enzyme (CPK).
- EMG findings.
- Muscle biopsy.

N.B. In a typical case with skin lesion, muscle biopsy is not essential. But in idiopathic polymyositis, muscle biopsy is necessary.

Q: How to treat dermatomyositis or polymyositis?**A:** As follows:**1. General measures:**

- Patient's education and reassurance.
- Physiotherapy.
- Bed rest in severe case.
- Avoidance of sunlight and use of sunscreen.

2. Drug therapy:

- Prednisolone 0.5 to 1 mg/kg daily to induce remission. Continued for 1 month after myositis is clinically and enzymatically inactive. Taper slowly. Maintenance dose is 5 to 7.5 mg daily. May be required for months, even years.
- If severe respiratory or pharyngeal weakness: Methylprednisolone 1 g daily for 3 days.
- If no response to steroid: methotrexate or azathioprine may be given.
- If methotrexate and azathioprine fail: cyclosporine or cyclophosphamide or mycophenolate mofetil may be tried.
- High dose IV immunoglobulin may help in refractory cases.
- Rituximab may be used, if all fail.

3. Treatment of underlying malignancy may improve the condition.**Q: What is the prognosis?****A: As follows:**

- 5-year survival in treated patient is >95%, 10 year survival is 84%.
- Worse prognosis if severe at presentation, delay of treatment, severe dysphagia or respiratory difficulty, older patient and if there is underlying malignancy.
- Dermatomyositis responds better than polymyositis. So better prognosis.

PROXIMAL MYOPATHY

Instructions by the examiner

- Test for proximal myopathy.
- Examine the lower limbs or upper limbs.

Proceed as follows:

1. In the upper limbs:
 - Ask the patient to raise the arms above head (patient is unable to do so).
 - Ask the patient to sit, abduct the arm (patient is unable), outstretch the arm in front (patient is unable), keep the arm on the side at 90° and press against resistance (in positive case, there is less power).
2. In the lower limbs:
 - While the patient is lying flat, ask him to raise the lower limbs (patient may be unable to do so).
 - Press the knee and ask the patient to raise the limbs against resistance (patient may be unable to do so).
 - Ask the patient to sit on the floor in squatting position. Then ask him to stand up (patient is unable to do so).
 - Ask the patient to walk (see the gait).

Presentation of a Case:

- This patient has difficulty in raising both the arms above the head and weakness of both arms as well.
- He has also difficulty in raising upwards of both lower limbs and difficulty in standing from sitting.

My diagnosis is **Proximal myopathy** (both upper and lower limbs).

Q: What are the **complaints or presentations** of the patient?

A: The patient may complain of difficulty in combing, climbing upstairs and raising from the chair or squatting (also features of primary diseases may be present).



Unable to raise both arms



Proximal myopathy (wasting shown, severe)



Proximal myopathy (wasting shown, early stage)

Q: What are the causes of proximal myopathy?**A:** As follows:

- Dermatomyositis or polymyositis.
- Myasthenia gravis.
- Myasthenic myopathic syndrome (Eaton–Lambert syndrome).
- Myopathy (limb girdle, fascio-scapulo-humeral and mitochondrial, except myotonic dystrophy).
- Cushing's syndrome.
- Diabetic amyotrophy.
- Thyrotoxicosis (also hypothyroidism).
- Polymyalgia rheumatica.
- Osteomalacia.
- Hyperparathyroidism.
- Periodic paralysis.
- Alcohol and drugs (steroid, chloroquine, amiodarone, lithium, zidovudine).
- McArdle's syndrome (myophosphorylase deficiency. In such case, there is stiffness and cramps of muscle after exercise, which is hard and painful on movement).

Q: What are the causes of painful muscle?**A:** As follows:

- Physiological (after heavy exercise).
- Polymyositis or dermatomyositis.
- Polymyalgia rheumatica.
- Fibromyalgia syndrome.
- Viral infection.
- Chronic alcoholism.
- Following convulsion.
- Associated with rheumatological disease.
- Functional.

Q: What are the causes of acute or sudden muscular weakness?**A:** As follows:

- Guillain–Barré syndrome.
- Hypokalaemia and hyperkalaemia.
- Familial periodic paralysis.
- Thyrotoxic periodic paralysis.
- Functional (hysterical conversion reaction).

Q: What are the drugs causing myopathy?**A:** Steroid, penicillamine, hydroxychloroquine or chloroquine, statins (lovastatin, simvastatin), zidovudine.

Q: What is Eaton–Lambert syndrome?

A: It is a paraneoplastic syndrome characterized by proximal muscle weakness and wasting due to defective acetylcholine release at the neuromuscular junction. It commonly involves the lower limb, but may involve any muscle. Causes are:

- There is defect in **acetylcholine** release at the neuromuscular junction due to auto-antibody against pre-junctional voltage gated calcium channel at the motor nerve terminal. Small cell carcinoma of lung may trigger the auto-antibody reaction.
- Commonly due to small cell carcinoma of lung, may be associated or precede the manifestations of carcinoma.

Clinical features:

- Proximal weakness, common in lower limbs but any muscle may be involved.
- Ptosis and diplopia occur in 70% cases.
- Reflexes are absent or diminished.
- Muscle power may be increased and tendon reflexes may return after repeated activity or sustained contraction of the relevant muscle (reverse of myasthenia gravis).
- There may be autonomic dysfunction (dry mouth, constipation, impotence).

N.B.: Abnormality of reflex, muscle power and autonomic disturbance are absent in myasthenia gravis.

Investigations:

- EMG shows progressive incremental response (reverse of myasthenia gravis where there is decremental response).
- Antibody to P/Q type voltage gated calcium channel (anti-VGLC), found in 90% cases.
- Chest X-ray, CT scan or MRI to exclude malignancy, if suspected.

Treatment: Depends on cause. For symptomatic relief, the following treatment may be given:

- 3, 4 diaminopyridine may be given.
- IV immunoglobulin may be helpful.
- Pyridostigmine may give symptomatic relief.
- Plasmapheresis.
- Treatment of the primary cause.

GOUT

Instruction by the examiner:

- Examine the hands or feet. Or, look at here. What is it? (Tophus). What else do you like to like to examine?

Look at the following points carefully (in hands):

- Any deformity of joints or swelling of hands (symmetrical or asymmetrical).
- Presence of tophi (with skin necrosis, chalky or pasty material).
- Look for tophi in other parts (helix of ear, extensor and ulnar surface of forearm, olecranon bursa, dorsum of hands and fingers, Achilles tendon).

Presentation of a Case (in Hands): Case No. 1

- The patient has deformity with swelling of DIP joints, involving the fingers of right (or left) hand and also other small joints (mention which one).
- There is a tophus with necrosis over it with whitish or chalky discharge.

My diagnosis is **Gout** (if tophus is present, diagnosis is **Chronic tophaceous gout**).

Q: What relevant findings do you want to see in gout?

A: As follows:

- Liver and spleen (enlarged in lymphoma, myeloproliferative or lymphoproliferative disease).
- Lymph nodes (enlarged in lymphoma).
- Evidence of psoriasis (there may be skin lesion and nail change).
- Evidence of chronic renal failure.
- Evidence or features of hypothyroidism.
- History of hypertension, diabetes mellitus, ischaemic heart disease and drugs (see below).

Q: Which joints are involved in gout?

A: As follows:

- MTP (metatarsophalangeal) joint of great toe >50% cases (called podagra).
- Other joints are ankle, mid-foot, knee, small joints of hand, wrist and elbow.



Swelling and redness of right 2nd MCP joint



Tophi in 2nd DIP joint



Gout affecting elbow



Tophus (confuses with Heberden's node)

Q: What are the **differential diagnoses** of gout?

A: As follows:

- Traumatic.
- Septic arthritis.
- Pseudogout.
- Psoriatic arthritis.
- Reiter's syndrome.

Differential diagnoses of **chronic gout** are:

- Pseudogout.
- Osteoarthritis.
- Psoriatic arthritis.
- Rheumatoid arthritis.
- Tuberculous arthritis.

Presentation of a Case (in Foot): Case No. 2

- There is swelling, redness and tenderness of metatarso-phalangeal joint of great toe, other joints are also involved.
- There is a tophus with necrosis over it with whitish or chalky discharge.

My diagnosis is **Gout** (if tophus is present, diagnosis is **Chronic tophaceous gout**).

Q: What is **tophus**?

A: Nodular, hard and irregular swelling due to deposition of urate with inflammatory cells surrounding them (tophus means chalk stone). It indicates chronic gout. Patient with severe tophaceous disease appear to have milder or less frequent acute attack than non-tophaceous patients. Tophus may have area of necrotic or ulcerated skin over it and may exude chalky material containing monosodium urate crystal. Tophus resolves slowly by treatment of hyperuricaemia.

Tophus may be confused with:

- Rheumatoid nodule.
- Tendon xanthoma.
- Neurofibroma.
- Lipoma.



Tophus (helix of ear)



Acute gout



Podagra



Chronic tophaceous gout

READ THE FOLLOWING TOPICS IN RELATION TO GOUT

Q: What is **gout**? What are the **types**?

A: Gout is a disorder of purine metabolism characterized by hyperuricaemia associated with the deposition of monosodium urate monohydrate (MSUM) crystals giving rise to arthritis, tenosynovitis, bursitis and tophaceous deposit. It is 2 types:

- Primary: common in males, above 40 years.
- Secondary: common in females, above 65 years.

Q: What is **pseudogout**?

A: It is a crystal arthropathy caused by deposition of calcium pyrophosphate dihydrate (CPPD), also called chondrocalcinosis. Examination of synovial fluid under polarized light shows rhomboid shaped and positively birefringence CPPD crystals.

Causes of hyperuricaemia and gout:

1. Defect in renal excretion:

- Renal failure.
- Drugs: diuretic (thiazide), low dose aspirin, pyrazinamide, ethambutol, nicotinic acid, ethanol, cytotoxic drug, cyclosporine, alcohol.
- Hyperparathyroidism.
- Myxoedema.
- Chronic lead poisoning.
- Down's syndrome.
- Lactic acidosis (due to alcohol, starvation, toxemia of pregnancy and type I glycogen storage disease).

2. Excess production of uric acid:

- Myeloproliferative disease.
- Lymphoproliferative disease.
- Psoriasis.
- Excess purine synthesis (hypoxanthine-guanine phosphoribosyltransferase deficiency, glucose-6-phosphatase deficiency).
- Idiopathic (common).

Q: Could uric acid be **normal** in acute gout?

A: Yes, hyperuricaemia is common but not invariable. Usually, 5% of hyperuricaemic patients develop gout.

Q: What are the **precipitating factors** of acute gout?

A: Acute attack may be precipitated by:

- Sudden rise of uric acid: Dietary excess or severe dietary restriction, alcohol, diuretic (thiazide).
- Sudden fall of uric acid by allopurinol or uricosuric drug.
- Others: Trauma, surgery and severe exercise.

Q: How does the patient usually **present with acute gout**?

A: In typical acute attack:

- Severe excruciating pain, mainly in metatarso-phalangeal joint of great toe, usually in early morning or late night, awaking the patient from sleep. Other joints are also involved.
- The joint is red, swollen and tender.

Q: What investigations should be done in gout?**A:** Diagnosis is clinical.

- CBC: ESR (high). Leukaemia should be excluded (may cause high uric acid).
- Serum uric acid.
- CRP (high).
- To be confirmed—aspiration from joint, bursa or tophus to see MSUM crystals under polarized microscope. It looks needle shaped and negatively birefringence crystals (but in pseudogout, CPPD crystals are rhomboid and positively birefringence). It is intracellular (in leucocytes) in acute cases, may be extracellular.
- Other investigations: urea and creatinine (to exclude CKD), blood sugar, lipid profile, thyroid function (to exclude hypothyroidism).

Q: What is the role of serum uric acid level to diagnose acute gout?**A:** It has little value as in acute gout, serum uric acid may be normal. Asymptomatic hyperuricaemia is more common.**Q: How to treat acute gout?****A:** As follows:

1. For pain: NSAID (indomethacin, naproxen, diclofenac oral or suppository).
2. If no response: colchicine 1 mg loading dose, then 0.5 mg every 6 hours till relief of symptoms (side effects are nausea, vomiting, diarrhoea and abdominal pain).
3. In severe arthritis with effusion: aspiration and intra-articular steroid (methylprednisolone) may be given.
4. Prevention:
 - Dietary restriction: Avoid uric acid containing diet (liver, kidney, brain, red meat, cabbage, cauliflower, carrot and spinach). Severe calorie restriction should be avoided. However, no need of strict specific dietary restriction.
 - Avoid alcohol and starvation.
 - Reduction of weight in obese patients (slow reduction).
 - Avoid precipitating drugs.
 - Allopurinol may be given.
 - Febuxostat, a non-purine analogue inhibitor of xanthine oxydase is also helpful.
 - Hypouricaemic drugs should not be given in acute attack, may be started after several weeks of acute attack.

Indications of hypouricaemic drug therapy:

- Recurrent attack of gout.
- Presence of tophi.
- Radiological evidence of joint damage.

Uricosuric drugs: Probenecid, sulphinpyrazone (high-dose aspirin and indomethacin may be uricosuric). Uricosuric drugs may be helpful if:

- No renal failure.
- Creatinine clearance >80 ml/min (if <80 ml/min, less effective. If <30 ml/min, it has no effect).
- Urine uric acid <700 mg/day on general diet.

Uricosuric drugs are **contraindicated** in:

- Gout with overproduction of uric acid and gross uricosuria.
- Renal failure.
- Urate lithiasis.

Allopurinol: Drug of choice. It inhibits the production of uric acid by inhibiting xanthine oxidase, responsible for conversion of xanthine and hypoxanthine to uric acid. Dose is 100 to 300 mg/day. In renal failure or old age, start with low dose (100 mg). Allopurinol should not be given in acute attack and is usually given several weeks after the acute attack. If given, it may precipitate acute attack. To prevent, NSAID or colchicine (0.5 mg 12 hourly) should be used together.

After allopurinol, uric acid should come down to half of the normal stage. Dose should be gradually increased, until this value is achieved. Drug should be continued indefinitely.

Febuxostat: It is a non-purine analogue inhibitor of xanthine oxidase, well tolerated and as effective as allopurinol. It is safer in renal impairment, as it undergoes hepatic metabolism rather than renal excretion. It is helpful in patients who cannot tolerate allopurinol. Dose is 80 to 120 mg. Side effects are nausea, diarrhoea, arthralgia, headache, increased hepatic serum enzyme levels and rash. It may increase cardiovascular risks.

Q: What is uric acid nephropathy?

A: It means renal impairment is secondary to hyperuricaemia. There may be chronic renal failure, acute renal failure (due to obstructive uropathy) and nephrolithiasis. Nephropathy is due to:

- Urate deposition in renal parenchyma.
- Renal tubular obstruction and uric acid stone formation.

ASYMPTOMATIC HYPERURICAEMIA:

1. It is 10 times more common.
2. No treatment is required in majority of the cases.
3. A search should be made to find out the secondary cause of hyperuricaemia.
4. Reduction of weight, avoidance of uric acid containing diet, alcohol and smoking.
5. Indication of treatment in asymptomatic hyperuricaemia:
 - If it is symptomatic.
 - 24 hours urine uric acid >1,100 mg/day.
 - Strong family history of gout, urate stone or renal failure or persistent high uric acid >10.1 mg.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Instruction by the examiner:

- Look at the face. What are your findings? What else do you want to see?
- Perform the general examination of this patient.

Presentation of a Case:

- This patient has erythematous and scaly rash along the butterfly distribution and also in forehead.
- Some areas of scarring or depigmentation and telangiectasia are present.
- Face looks puffy and plethoric (due to steroid).

My diagnosis is **SLE**.

Q: What else do you want to see?

A: I want to see:

- Skin rash in the other parts of body.
- Mouth ulcer (sharply defined white patch with red margin).
- Alopecia (non-scarring).
- Arthropathy or arthritis.



Discoid lupus
erythematosus



Butterfly rash in
SLE



Arthritis of hand (SLE)



Skin rash (SLE)

Q: What history do you like to take in SLE?

A: I want to take the history of:

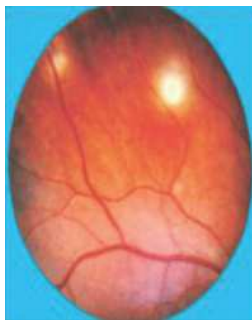
- Whether the rash is aggravated on exposure to sunlight (photosensitivity).
- Drugs (see below) and oral contraceptive pill (in female).
- Repeated abortions in female.
- Convulsion, depression and unconsciousness or paralysis or paresis.
- Raynaud's phenomenon (present in 20% cases).
- History of DVT or thromboembolism.
- Family history of SLE.



Mouth ulcer in SLE
(multiple)



Mouth ulcer in SLE



Fundoscopy
(Cytoid body)



Alopecia

Q: What are your **differential diagnoses**? Or what are the **causes** of butterfly rash?

A: As follows:

- SLE (or DLE).
- Dermatomyositis.
- Mixed connective tissue disease.
- Systemic sclerosis.
- Sarcoidosis.
- Drug rash.

READ THE FOLLOWING TOPICS IN RELATION TO SLE

Q: What is **SLE**?

A: It is an autoimmune chronic multi-system disease characterized by production of multiple auto-antibodies, immune complexes and widespread immune-mediated organ damage.

Q: From where is the **name SLE** derived?

A: Lupus means wolf. SLE is named because of erosive nature of disease that looks like damage caused by wolf's bite.

Q: What are the **diagnostic criteria** of **SLE**?

A: There are 11 clinical criteria and 6 immunologic criteria. If ≥ 4 criteria (at least 1 clinical and 1 immunologic) *or* biopsy proven lupus nephritis with positive ANA or anti-ds DNA, it is diagnostic of SLE.

Clinical criteria:

1. Acute Cutaneous Lupus OR Subacute Cutaneous Lupus:

- **Acute Cutaneous Lupus:** Malar rash/butterfly. Fixed erythema, flat or raised, over the malar eminences, sparing nasolabial folds. Bullous lupus, toxic epidermal necrolysis variant of SLE, maculopapular, photosensitive rash,
- **Subacute cutaneous lupus:** non-indurated psoriasiform and/or annular polycyclic lesions, resolve without scarring.

2. **Chronic cutaneous lupus:** Discoid rash, erythematous raised patches with adherent keratotic scales and follicular plugging $\pm$ atrophic scarring. Erythema, pigmented hyperkeratotic oedematous papules, atrophic depressed lesions.
3. **Non scarring alopecia:** In the absence of other causes.
4. **Oral/nasal ulcers:** In the absence of other causes.
5. **Synovitis:** Involving 2 or more joints or 2 or more tender joints with >30 minutes of morning stiffness.
6. **Serositis**, in the absence of other causes:
 - a) Lung (pleurisy for >1 day, or pleural effusions, or pleural rub)
 - b) Pericardial pain for >1 day, or pericardial effusion, or pericardial rub, or pericarditis on ECG.
7. **Urine analysis:** Presence of proteinuria (>0.5 gm/day) or red cell casts.
8. **Neurological features:** Seizures, psychosis, mononeuritis multiplex, Myelitis, peripheral or cranial neuropathy; cerebritis/acute confusional state in absence of other causes.
9. **Haemolytic anaemia.**
10. **Leucopenia:** (WCC $<4000/\text{mm}^3$) At least once, or lymphopenia (lymphocytes $<1000/\text{mm}^3$) at least once.
11. **Thrombocytopenia:** (Platelets $<100,000/\text{mm}^3$) At least once.

Immunologic criteria:

1. ANA (positive).
2. Anti-ds DNA (positive).
3. Anti-Sm (Smith) antibody (positive).
4. Serum anti-phospholipid antibody.
5. Low complements (C3, C4, CH50).
6. Direct Coomb's test (in the absence of haemolytic anaemia).

Q: What are the atypical features of SLE?

A: As follows:

- Raynaud's phenomenon.
- Chorea.
- Repeated abortion.
- Epilepsy or cerebrovascular disease (CVD) in young age.
- Psychiatric disorder.

Q: What are the manifestations or clinical feature of SLE? Or, what are the organs involved in SLE?

A: SLE is common in females, 20 and 30 years old, F:M = 9:1 (ratio is equal in children and elderly). Involves any organ of body.

1. General features:

- Fever.
- Arthralgia, arthritis (non-erosive), myalgia.
- Fatigue, tiredness, weakness, malaise, weight loss.
- Skin manifestation (80%): malar rash, discoid rash, photosensitivity, ulcer, vasculitic lesions on the finger tips and around the nail folds, livedo reticularis (in discoid lupus, only skin is involved).
- In skull, scarring alopecia, lupus hair (short broken hair above the forehead).

2. Heart (involved in 25%):
 - Pericarditis, pericardial effusion and myocarditis.
 - Rarely, non-infective endocarditis called Libman–Sacks endocarditis (common in anti-phospholipid syndrome). Mitral regurgitation may occur.
 - Increased incidence of IHD.
3. Vascular:
 - Raynaud's phenomenon.
 - Vasculitis.
 - Arterial and venous thrombosis (in anti-phospholipid syndrome).
 - Atherosclerosis.
4. Lungs (involved up to 50% cases):
 - Pleurisy, pleural effusion (may be bilateral) and pneumonitis.
 - Atelectasis and shrinking lung with elevation of diaphragm (shrinking lung syndrome).
 - Pulmonary fibrosis (rare, found in overlap syndrome).
 - Increased risk of pulmonary embolism.
 - Intrapulmonary haemorrhage with vasculitis (rare but dangerous).
5. Eyes:
 - Episcleritis, scleritis, conjunctivitis.
 - Optic neuritis (blindness is uncommon).
 - Secondary Sjögren's syndrome (dry eye and dry mouth) in 15% cases.
 - Retinal vasculitis can cause infarction (fundoscopy shows white, hard exudate called cytoid body).
6. GIT (rarely involved):
 - Mouth ulcer (usually painless, but may be painful if secondary infection).
 - Mesenteric vasculitis (may cause small bowel infarction or perforation).
 - Ascites.
 - Others: nausea, vomiting, diarrhoea, abdominal pain, mild hepatosplenomegaly.
7. Haematological:
 - Anaemia (normocytic normochromic) and Coombs positive auto-immune haemolytic anaemia.
 - Thrombocytopenia (often confused with ITP), leucopenia, neutropenia and lymphopenia.
8. Central nervous system (CNS):
 - Fatigue, headache, poor concentration.
 - Visual hallucination.
 - Chorea, epilepsy, migraine.
 - Cerebrovascular disease (CVD), paralysis.
 - Organic psychosis, depression.
 - Transverse myelitis.
 - Lymphocytic meningitis.
 - Cerebellar ataxia.
 - Cranial nerve palsy, peripheral neuropathy.
9. Kidney:
 - Glomerulonephritis (commonly proliferative, may be mesangial, focal or diffuse, membranous).
 - Nephrotic syndrome.
 - Renal vein thrombosis.
10. Others: Lymphadenopathy, infertility, abortion, menorrhagia.

Q: What is 'Chronic discoid lupus erythematosus' (CDLE)?

A: It is a variant of SLE in which the disease is mainly limited to the skin, characterized by photosensitivity, discoid rash, erythema, atrophic plaque, scaling, hypopigmentation, follicular plugging and telangiectasia. Scarring alopecia may occur. Oral involvement (erythematous patches or ulceration) occurs in 25% of cases. Raynaud's phenomenon or chilblain-like lesions (chilblain lupus) occur rarely. F: M = 2:1 (in SLE 9:1). SLE may occur in 5% cases (more in children). ANA is positive (30% cases), anti-ds DNA is negative and complements are normal. **Treatment is as follows:**

- Use of sunscreen and topical steroid.
- Hydroxychloroquine, 200 to 400 mg/day.
- In resistant cases or if associated arthritis: prednisolone or immunosuppressant may be given.

Q: What is SCLE (subacute cutaneous lupus erythematosus)? How to treat?

A: It is characterized by scaly red patch or circular, flat, red lesions (confused with psoriasis) on the upper torso and upper limbs, highly photosensitive. Arthralgia and mouth ulceration may be present but significant organ involvement is rare. Most patients have positive anti-Ro (SSA), anti-La (SSB) and ANA. **Treatment is as follows:**

- Oral dapsone.
- Hydroxychloroquine.
- Systemic immunosuppressants (prednisolone or ciclosporin) in some case.

Q: What are the drugs causing SLE? What are the features of drug-induced SLE? How to treat such case?

A: Hydralazine (90%, slow acetylator), procainamide (rapid acetylator), anticonvulsant (carbamazepine, phenytoin), phenothiazine, isoniazid, oral contraceptive pill, ACE inhibitor, penicillamine, methyl dopa, minocycline. **Features are:**

- Sex ratio: equal.
- Lung involvement is common, but renal and neurological involvements are rare.
- ANA is usually positive.
- Anti-ds DNA is negative.
- Complements are normal.
- Anti-histone antibody is positive in 95% cases (characteristic, but not specific).
- Drugs causing SLE-like syndrome usually do not aggravate primary SLE.
- Clinical features and laboratory abnormalities become normal when offending drugs are stopped.

Treatment: Withdrawal of drugs. Short course steroid (prednisolone) may be necessary.

Q: What is the cause of abdominal pain in SLE?

A: As follows:

- Mesenteric vasculitis or perforation of gut.
- Peptic ulcer as a complication of steroid therapy.
- Perisplenitis or splenic infarction.
- Pancreatitis.

Q: What is the type of arthritis in SLE?

A: Usually non-erosive and non-deforming. Rarely, deformity may occur similar to rheumatoid arthritis, called Jaccoud's arthritis. Aseptic or avascular necrosis of head of femur may occur.

Q: What is the cause of **avascular necrosis** of head of femur in SLE?

A: It is due to:

- Vasculitis in SLE.
- Prolonged use of steroid (actual cause of necrosis due to steroid is unknown. Probably steroid causes hypertrophy of lipocytes, which compresses blood vessels, leading to ischaemic necrosis of bone).

Q: What is the cause of **backache** in SLE?

A: Avascular necrosis.

Q: What is **avascular necrosis**? Where is it **involved**?

A: Avascular necrosis is the ischaemic necrosis of bone. It commonly involves the head of femur, also knee, shoulder.

Q: What **auto-antibodies** are found in SLE?

A: As follows:

- ANA (positive in 95% cases).
- Anti ds-DNA (highly specific, but positive in 30 to 60% cases).
- Anti-Smith (Anti-Sm) antibody (highly specific, positive in 10 to 25% cases).
- Anti-Ro (SSA, positive in 40% to 60%) and anti-La (SSB, positive in 15%).
- Anti-Phospholipid antibody (positive 25% to 40% cases).
- Ant-Histone antibody (positive in drug induced SLE, but not specific).

Q: What **investigations** should be done in SLE?

A: As follows:

1. CBC (Shows anaemia, leucopenia, thrombocytopenia, lymphopenia and high ESR).
2. Urine (Shows proteinuria, haematuria, RBC or granular cast). If proteinuria, 24 hour urinary protein should be done.
3. CRP (It is normal. Increased CRP indicates infection).
4. ANA (positive in 95% cases. It is the most sensitive screening test).
5. Anti-ds DNA (positive in 30 to 60% cases. It is highly specific for SLE).
6. Anti-Sm (Smith) antibody (positive in 10 to 25% cases).
7. Complements (C3 and C4 are low in active disease).
8. Immunoglobulin (high titre of IgM and IgG).
9. Serum anti-phospholipid antibody.
10. Others (these indicate presence of antiphospholipid antibody):
 - VDRL (false positive).
 - Platelet (low).
 - Prothrombin time (prolonged).
 - APTT (prolonged, not corrected by addition of normal plasma).
11. Skin biopsy (from normal skin and skin lesion for histopathology and DIF):
 - Biopsy of normal skin for direct immunofluorescence test: shows deposition of immune-complex at dermo-epidermal junction (called lupus band). Biopsy specimen of normal skin for DIF should be sent in normal saline soaked gauge (not in formalin, as protein is denatured by formalin).
 - Biopsy skin lesion for histopathology: biopsy specimen should be taken in formalin.
12. If renal involvement: 24 hours urinary protein, serum urea and creatinine, creatinine clearance rate (CCR), renal biopsy.
13. If CNS involvement: EEG, CT or MRI.

Q: How to treat SLE?**A:** As follows:**1. General measures:**

- Explanation and education regarding the nature of the disease.
- Reassurance and psychological support.
- Avoidance of UV light exposure, use of sun blocks.
- Cardiovascular risk factors like hypertension and hyperlipidaemia should be controlled. Smoking should be stopped.

2. Drug therapy:

- Mild cases: NSAID (if fever, arthralgia, headache). Chloroquine or hydroxychloroquine (in skin lesion, arthritis, arthralgia, serositis without organ involvement). Short course steroid (in skin rash, synovitis, pleuro-pericarditis).
- In severe and active disease: Steroid should be given.
- Acute life-threatening SLE affecting kidney, CNS or CVS, haemolytic anaemia, thrombotic thrombocytopenia: high dose steroid and immunosuppressive drug. Pulse methylprednisolone (500 mg to 1 gm IV) daily for 3 to 5 days, followed by oral prednisolone. Cyclophosphamide (2 mg/kg IV) may be given.
- In renal involvement: (see below).

Steroid (prednisolone):

Indications:

- In mild disease, not responding to chloroquine and NSAID.
- Severe and active disease with involvement of vital organ (heart, kidney, CNS, haematological abnormality).

Dose:

- Without major organ involvement: 0.25 to 0.5 mg/kg/day.
- Major organ involvement: 1 to 1.5 mg/kg/day.

Dose schedule of steroid (one suggested regimen):

- Initially, full dose (45.0 to 60.0 mg daily) for 4 to 8 weeks.
- Then, reduce 10.0 mg weekly till 30.0 mg,
- Then, 25.0 mg/day for 1 week.
- Then, 20.0 mg/day for 1 week.
- Then, 15.0 mg for 1 month.
- Then, reduce 2.5 mg every 2 weekly as follows—
 - Alternate First day 15.0 mg, second day 12.5 mg to 2 weeks.
 - First day 15.0 mg, second day 10.0 mg to 2 weeks and so on (until no prednisolone in 2nd day).
 - Then, 15.0 mg on alternate day (continue and follow up).

Q: How long steroid should be continued? Or, when steroid should be stopped?

A: When the disease activity (both clinically and biochemically) disappears, steroid should be reduced slowly over months and can be withdrawn (may be needed to continue for 2 to 3 years. For lupus nephritis, treatment is usually given for 5 years.

Methylprednisolone: Given in severe SLE with carditis, renal and cerebral involvement, poor general condition.

- Dose: 500 mg to 1 gm mixed with 200 mL 5% DA, IV daily for 3 to 5 days, followed by prednisolone 1 mg/kg for 6 to 10 weeks, then gradual tapering (as above).

Cyclophosphamide: Given in renal lupus (classes III, IV and V), severe renal disease as evidenced by (UTP >1 g, raised serum creatinine and decreased creatinine clearance), CNS involvement. Given as follows:

- 0.5 to 1 g/m² body surface. It is given monthly as a pulse therapy IV with 500 mL fluid (every month for six cycles, then every 3 months for another six cycles or till the disease is inactive for 1 to 2 years). Then hydroxychloroquine or azathioprine can be started.
- Alternately, cyclophosphamide 250 mg/m² body surface, every 15 days for 12 doses, followed by prednisolone as maintenance therapy.
- After 12 weeks of cyclophosphamide, oral azathioprine (2 to 2.5 mg/kg daily) may be given.

N.B. Remember the following:

- *Advantages of azathioprine: no gonadal toxicity and no adverse effect on pregnancy.*
- *Cyclophosphamide can cause gonadal toxicity, amenorrhoea, sterility, premature menopause and sometimes, leukaemia may occur. Moreover, it cannot be continued in pregnancy.*
- *Periodic blood count should be done initially 2 weekly, then monthly.*

Q: What is the **mechanism of haemorrhagic cystitis**? How to **prevent** this?

A: Cyclophosphamide can cause haemorrhagic cystitis (more by oral route). It is due to production of **acrolein**, a metabolite from cyclophosphamide that is highly toxic to the mucosa of urinary bladder.

This can be prevented by:

- Plenty of fluid (3 to 4 L).
- Using mesna (0, 4 and 8 hours of therapy).
- Advise to the patient: to micturate frequently.

Prognosis in SLE:

- 10 year survival is 90%, but this is lower if vital organs are involved (heart, kidney, lung, CNS).
- Mortality shows bimodal pattern. In early age, death is usually due to infection (mostly opportunistic), renal or cerebral disease. In later age, accelerated atherosclerosis is common, incidence of myocardial infarction is 5 times more than in general population (so, risk factor for atherosclerosis should be controlled, such as avoid smoking, control hypertension, obesity, hyperlipidaemia etc.).
- In the long term, some patients may develop cancers, especially lymphoma.
- Rarely, there may be deforming arthritis, chronic progressive destruction of joints and osteoarthritis.

BRIEF NOTES ON MCTD

Mixed connective tissue disease is a group or combination of features of systemic sclerosis, SLE and polymyositis (or other collagen disease, e.g., rheumatoid arthritis). It is also called overlap syndrome. **Clinical features are:**

- Common in females, third to fourth decade, rare in children and elderly.
- Patient usually presents with Raynaud's phenomenon, muscular pain or weakness, swollen, oedematous hands and fingers. Later, features like sclerodactyly, calcinosis, cutaneous telangiectasia.
- Skin rash of SLE or dermatomyositis. Sjögren's syndrome, may develop later
- Lung involvement occurs in 85% cases, but frequently asymptomatic. Carbon monoxide transfer is diminished. Pleurisy is common. Pulmonary fibrosis may occur. Pulmonary hypertension is the common cause of death.
- Renal disease occurs in 25%, gastrointestinal involvement occurs in 70% cases.
- In heart, pericarditis (30%), myocarditis, arrhythmia, mitral valve prolapse may occur.

Investigations:

1. Anti-RNP antibody: high.
2. ANA: positive with a speckled nucleolar pattern.
3. Anti-scl 70: may be positive.
4. CPK: may be high.
5. Other investigations: CBC and ESR (high), X-ray chest (shows reticulonodular shadow), barium swallow, skin biopsy.

Treatment: Prednisolone, which responds quickly. 10 years survival in 80% cases.

RENAL INVOLVEMENT IN SLE

Q: What are the features of renal involvement in SLE?

A: Renal involvement occurs in 1/3rd of SLE, 25% develop end stage renal failure within 10 years. Lupus nephritis is classified histologically by WHO criteria.

Type	Histology	Clinical Features
Type I	Minimal mesangial lupus nephritis (LN), normal on light microscopy	Asymptomatic
Type II	Mesangial proliferative LN with mesangial hypercellularity and matrix expansion.	Mild renal disease
Type III	Focal LN (involving <50% glomeruli). Subepithelial deposits seen.	Haematuria and proteinuria
Type IV	Diffuse LN (involving >50% glomeruli). There are segmental and global lesions as well as active and chronic lesions. Subendothelial deposits are present.	Progression to nephrotic syndrome, hypertension and renal insufficiency. It is common and most severe form of LN.
Type V	Membranous LN, occurs in 10 to 20% patients. Can occur in combination with type III and IV.	Heavy proteinuria (NS), haematuria, hypertension. Good prognosis.
Type VI	Advanced sclerosing LN. It causes sclerosis of >90% glomeruli.	Progressive renal failure. Severe form.

Q: How to diagnose renal involvement in SLE?

A: Patient may present with nephrotic syndrome or acute nephritic illness or renal failure (either AKI or CKD).

Renal involvement is diagnosed by:

1. Urine:
 - Proteinuria (+ + +), haematuria and granular or RBC cast.
 - UTP (24 hours urinary total protein) >0.5 gm.
2. Blood:
 - Urea and creatinine (high).
 - Creatinine clearance rate (CCR): low.
3. USG.
4. CT scan in some cases.
5. Renal biopsy.

Q: How to treat renal lupus?

A: According to histological type:

- Type I: No treatment.
- Type II: Benign. But sometimes, steroid may be needed.
- Type III, IV and V: Immunosuppressive therapy with steroid and cyclophosphamide or mycophenolate mofetil is used for induction. Then azathioprine and mycophenolate mofetil are used for maintenance.
- Rituximab (anti-CD20) may be used in some patients.
- Symptomatic treatment for hypertension and oedema.

N.B.: Remember the following:

- *Focal glomerulonephritis respond well to treatment with prednisolone 40 to 60 mg/day.*
- *Diffuse and membranous lesions do not respond well to steroid only. Pulse therapy with methylprednisolone for 3 days followed by maintenance with prednisolone is necessary. Sometimes azathioprine 2 to 3 mg/kg body weight or cyclophosphamide 100 to 150 mg daily with prednisolone may be given.*
- *Pulse therapy: IV cyclophosphamide is more effective than pulse methylprednisolone alone. Also combination therapy is sometimes more effective. Continuing IV treatment, quarterly for 1 year after renal remission decreases the risk of renal flare.*
- *Prognosis is better in type I, II and V.*

PREGNANCY WITH SLE

- Pregnancy is not contraindicated in SLE provided the disease is in control.
- Before pregnancy, the disease should be in remission. If SLE is inactive for 12 to 18 months prior to conception, there usually no activation of SLE in pregnancy.
- Pregnancy should be avoided if neurological, renal or cardiac abnormalities are present.
- If renal involvement and anti-phospholipid antibody is present, foetal loss is greater than 25%.
- Remission and exacerbation may occur in pregnancy (in 1st trimester) and also in puerperium.
- Relapse is more in fertile woman.

- In mother, if '**anti-Ro antibody**' (SSA) is positive, congenital complete heart block of baby due to transplacental transfer of this antibody. If **anti-Ro or anti-La (SSB)** antibodies is positive, 2% risk of SLE in baby.
- If mother has anti-phospholipid antibody, repeated abortions are common, also IUGR.
- Barrier method should be used rather than oral contraceptive which may aggravate SLE.

Complications of pregnancy in SLE:

- Abortion and still birth (10 to 30%).
- Preterm baby.
- IUD.
- IUGR.
- Premature labour.
- Perinatal death.
- Peri-partum or post-partum haemorrhage.
- Maternal death is rare. Death rate is more if renal involvement.
- Mother may develop hypertension and proteinuria. This may be confused with PET (In PET, there is no arthritis, no skin changes and no renal, cardiac, CNS symptoms. To confirm, ANA and anti-ds DNA should be done. If the patient already have SLE and develops PET, it is difficult to differentiate between these. However, in PET, there is no RBC cast and also C₃ is not low).

SLE in baby:

- Neonatal SLE is due to transplacental transfer of maternal anti-Ro (SSA) or anti-La (SSB) antibodies.
- The baby may have skin rash, hepatitis, congenital heart block, thrombocytopenia (due to antiplatelet antibody) and haemolytic anaemia. All features are transient.
- Congenital heart block is mostly asymptomatic but heart failure and hydrops foetalis may occur.

Treatment of SLE in pregnancy—

- There is no difference of treatment in pregnant and non-pregnant females.
- Prednisolone is the drug of choice in pregnancy. It is safe in pregnancy and does not cause any foetal abnormality. Even in inactive disease, prednisolone 10 mg/day should be given (dexamethasone or beclomethasone should be avoided).
- Low dose aspirin should be given in patients with antiphospholipid syndrome. Also heparin may be used.
- If prednisolone alone is not effective, prednisolone and azathioprine may be used.
- Anti-malarial drug is contraindicated in pregnancy because of foetal ototoxicity.
- Cyclophosphamide is contraindicated.

Dose of Prednisolone:

- If skin rash and arthritis: 5 to 20 mg/day.
- Pleuro-pericarditis: 0.5 to 0.8 mg/kg/day.
- CNS, renal and blood dyscrasia: 1 to 2 mg/kg.
- Prednisolone should be continued 4 to 6 weeks after delivery to avoid flares.
- Breast feeding is safe up to 30 mg/day in lactating mother.

ANTI-PHOSPHOLIPID SYNDROME

Anti-phospholipid syndrome is characterized by the presence of anti-phospholipid antibody. It is associated with recurrent arterial or venous thrombosis, recurrent foetal loss, thrombocytopenia. Some patients with anti-phospholipid antibody may not get anti-phospholipid syndrome. It is positive in SLE and may be found in many other cases. May be positive without any cause, called primary anti-phospholipid syndrome. 2 types of anti-phospholipid antibody:

- Anticardiolipin antibody: may be IgG or IgM. IgG is more pathogenic.
- Lupus anticoagulant: it interferes with phospholipid dependent coagulation tests.

In some patients, only one of these is positive and in others, both are positive.

Presence of anti-phospholipid antibody is associated with:

- Thrombosis, venous or arterial, 17% of stroke <45 years of age is thought to be due to anti-phospholipid antibody.
- Recurrent abortion or intrauterine growth retardation.
- Haematological: thrombocytopenia and auto-immune haemolytic anaemia.
- Neurological: epilepsy, TIA, stroke, migraine and chorea.
- Heart: sterile endocarditis (Libman–Sacks).
- Renal involvement with proteinuria and lupus nephritis (membranous).
- Skin: ulceration, livedo reticularis, gangrene and necrosis of digit.

Causes of anti-phospholipid antibody:

1. Primary: Thromboembolism without features of SLE.
2. Secondary: Causes are:
 - Rheumatological: SLE, DLE, RA, systemic sclerosis, Sjögren's syndrome, psoriatic arthropathy, dermatomyositis.
 - Vasculitis: Behcet's syndrome, temporal arteritis, Takayasu's arteritis.
 - Malignancy: bronchial carcinoma, renal cell carcinoma, prostatic carcinoma, thymoma, oesophageal carcinoma.
 - Haematological disease: leukaemia, lymphoma, myelofibrosis, polycythaemia, myeloma, monoclonal gammopathy.
 - Infections: HIV, infectious mononucleosis, rubella, parvovirus, hepatitis, TB, leprosy, infective endocarditis, Klebsiella, syphilis.
 - Drug induced: procainamide, phenothiazine.
 - Miscellaneous: diabetes mellitus, dialysis patient.

In <1% cases of anti-phospholipid syndrome, a severe type called catastrophic anti-phospholipid syndrome may occur. In such case, there may be diffuse thrombosis, thrombotic microangiopathy and multiorgan failure. It is treated with intravenous heparin, high dose steroid, intravenous immune globulin and plasmapheresis.

Investigations:

1. Serum antiphospholipid antibody (anticardiolipin and lupus anticoagulant).
2. Indirect tests for anti-phospholipid antibody:
 - Thrombocytopenia.
 - False positive VDRL.
 - Prolonged prothrombin time.
 - Prolonged APTT, which is not corrected by addition of normal plasma.

Treatment of anti-phospholipid syndrome:

- With thrombosis: Warfarin should be given and continued for life long.
- Without history of thrombosis, but with anti-phospholipid antibody only: Aspirin or clopidogrel may be given. Rarely warfarin may be needed.
- In pregnancy: Low dose aspirin and subcutaneous heparin should be started early in gestation. This reduces the chance of miscarriage, but pre-eclampsia and poor foetal growth remain common.
- Factor X inhibitor (rivaroxaban) may be considered.

N.B.: Remember the followings:

- *Persistently positive test (positive on at least 2 occasions ≤ 12 weeks apart) in 1 or more of these assays is needed to diagnose APS.*
- *However, some people test positive for APL will never develop APS, that is, not all positive APL are harmful.*

VASCULITIS

Instruction by the examiner:

- Perform the general examination. Or, Look at the foot or hand.

Presentation of a Case:

- There are few infarctions at the tip of great and second toe of right foot, also one small infarction at the tip of small toe of left foot.
- Multiple purpuric spots and few papular lesions are present on the front of both legs.
- Few areas of bruise and ecchymoses are also present.
- There is one small ulcer above the medial malleolus.
- Pulse is low volume (mention accordingly).

My diagnosis is **Vasculitis**.

Q: What else do you like to see?

A: I want to see any evidence of collagen disease like rheumatoid arthritis, SLE (butterfly rash, alopecia), history of fever, hypertension, heart (infective endocarditis), history of drug therapy.

N.B.: If vasculitis is associated with deformity of hand or foot joint, likely diagnosis is rheumatoid arthritis with vasculitis.



Vasculitis (toes)



Vasculitis (fingers)



Vasculitis (skin rash)

Q: What are the differential diagnoses?

A: As follows:

- Drug reaction.
- Collagen disease (SLE, rheumatoid arthritis, Wegener's granulomatosis).
- Microscopic polyarteritis (polyangitis).
- Cryoglobulinaemia.
- Buerger's disease.
- Henoch-Schönlein purpura.
- Sarcoidosis.
- Cutaneous amyloidosis.

Q: What are the diseases that mimic vasculitis?**A:** As follows:

- Infective endocarditis.
- Meningococcal septicaemia.
- Atrial myxoma.
- Anti-phospholipid syndrome.
- Malignancy.
- Cholesterol emboli.

Q: What is vasculitis?

A: Vasculitis syndrome is a heterogeneous group of disorders characterized by inflammation and necrosis of the walls of affected blood vessels, with associated damage to the skin, kidney, lung, heart, brain and gastrointestinal tract. Vasculitis may be primary in the absence of any cause or secondary to many inflammatory or infective diseases.

Q: What are the common causes of vasculitis?**A:** Causes of vasculitis depend on the type of artery affected.

1. Involvement of large artery:
 - Giant cell arteritis.
 - Polymyalgia rheumatica.
 - Takayasu's arteritis.
 - Behcet's disease.
2. Involvement of medium-sized artery:
 - Classical polyarteritis nodosa.
 - Buerger's disease.
 - Kawasaki's disease.
3. Involvement of small artery:
 - Immune complex mediated: Henoch–Schönlein purpura, essential cryoglobulinaemia, cutaneous leucocytoclastic vasculitis.
 - ANCA associated: Wegener's granulomatosis, Churg–Strauss syndrome, microscopic polyangiitis.
4. Other conditions associated with vasculitis:
 - Drug induced vasculitis.
 - Infective: infective endocarditis, chronic hepatitis B and C.
 - Collagen disease: rheumatoid arthritis, SLE, systemic sclerosis, polymyositis or dermatomyositis.
 - Goodpasture's syndrome.
 - Hypocomplementaemia.
 - Serum sickness.
 - Vasculitis with malignancy (paraneoplastic syndrome): lymphoma, hairy cell leukaemia.
 - Inflammatory bowel disease.

Q: How to classify vasculitis?**A:** As follow:

1. Cutaneous small vessel (post-capillary venule):
 - Idiopathic cutaneous small vessel vasculitis.
 - Henoch–Schonlein purpura.
 - Acute haemorrhagic oedema of infancy.
 - Urticarial vasculitis.
 - Cryoglobulinaemic vasculitis.
 - Drug induced.
 - Malignancy.
 - Connective tissue diseases.
 - Inflammatory bowel disease.
 - HIV infection.
 - Behcet's syndrome.
 - Sweet syndrome.
 - Erythema nodosum leprosum.
2. Medium vessel:
 - Polyarteritis nodosa.
 - Kawasaki's disease.
3. Mixed (medium and small) vessel disease:
 - Connective tissue disease (e.g., rheumatoid vasculitis).
 - Septic vasculitis.
 - ANCA associated—Microscopic polyangiitis, Wegener's granulomatosis, allergic granulomatosis (Churg–Strauss syndrome).
 - Drug induced (most are post-capillary venule only).
4. Large vessel vasculitis:
 - Giant cell arteritis.
 - Takayasu's arteritis.

Q: What are the common clinical features of vasculitis?**A:** As follows:

1. Constitutional symptoms: Fever, weight loss, malaise, arthralgia, arthritis, myalgia.
2. Features due multiple system involvement of the body:
 - Skin: painful palpable purpura, vesiculo-bullous lesions, urticaria, cutaneous nodules, ulcers, livedo reticularis, digital gangrene.
 - Eye: episcleritis, ulcer, visual loss.
 - Ear, nose, throat: epistaxis, nasal crust, recurrent sinusitis, deafness.
 - Respiratory: haemoptysis, cough, dyspnoea.
 - Cardiac: heart failure, angina or myocardial infarction.
 - Gastrointestinal: abdominal pain (due to chronic ischaemia or mucosal inflammation), mouth ulcer, diarrhoea.
 - Renal: proteinuria, haematuria, cast, acute or chronic renal failure.
 - Neurological: mononeuritis multiplex, sensory or motor neuropathy, fit, psychoses, confusion, stroke.
3. Secondary vasculitis: Features of the primary disease.

Q: What **investigations** should be done in vasculitis?

A: As follows:

- CBC, ESR (high).
- CRP (high).
- Urine for RME
- ANA, anti-ds-DNA, p-ANCA, c-ANCA.
- Biopsy of involved organ for histology and immunofluorescence.
- Angiography in some cases.
- Other investigations according to suspicion of cause

Q: How to **treat** vasculitis?

A: As follows:

- According to the cause.
- High dose steroid and immunosuppressive drugs are given in many cases.

OSTEOARTHRISIS

Instruction by the examiner:

- Look at the patient's hands or examine the hands of this patient.
- Examine the knee joint

Presentation of a Case (Hand):

- There are bony swellings at the proximal (Bouchard's nodes) and distal (Heberden's nodes) interphalangeal joints of both hands.
- DIP joints of both hands are swollen.

My diagnosis is **Osteoarthritis**.

(For knee joint osteoarthritis, see details examination of knee joint of this chapter).

Q: Why it is a case of **osteoarthritis**?

A: Because Bouchard's and Heberden's nodes are hallmarks of osteoarthritis.

Q: What are **Bouchard's and Heberden's nodes**?

A: As follows:

- Bouchard's node is the new bone formation at the proximal interphalangeal joint.
- Heberden's node is the new bone formation at the distal interphalangeal joint.

Q: What else do you want to see?

A: I want to examine other joints, especially the knee joints, ankles, cervical and lumbar spine.



Osteoarthritis of hands
(Heberden's Node)



Osteoarthritis of hands (Bouchard's
Node in PIP and Heberden's
Node in DIP joint)



Osteoarthritis of knees

Q: What is **osteoarthritis**?

A: It is a degenerative disease of the synovial joint characterized by focal loss of articular hyaline cartilage with proliferation of new bone and remodelling of joint contour. It is not inflammatory.

Q: What are the **types of osteoarthritis?****A:** 2 types:

1. Primary: unknown cause.
2. Secondary: to some other diseases, usually asymmetrical, commonly involves the weight-bearing joints. Causes are:
 - Trauma.
 - Congenital or developmental.
 - Inflammatory—rheumatoid arthritis, septic arthritis, gout, haemophilic arthritis.
 - Neuropathic joints (Charcot's joint).
 - Endocrine diseases—acromegaly, hyperparathyroidism.
 - Metabolic—haemochromatosis, alkaptonuria, Wilson's disease, chondrocalcinosis.

Q: What is **nodal osteoarthritis?**

A: It is a primary generalized osteoarthritis, which is autosomal dominant and occurs mainly in middle-aged women. There may be bilateral symmetrical involvement of many joints. Bouchard's and Heberden's nodes are typically found in nodal osteoarthritis. There is good functional outcome of the hands despite marked deformity.

Q: What are the **complications of osteoarthritis?****A:** As follows:

- Entrapment of nerves (ulnar nerve), carpal tunnel syndrome.
- Cervical spondylosis.
- Deformity.

Q: What typical **deformity may occur in the hand?**

A: Square hand due to subluxation of first metacarpophalangeal joint.

Q: In the hand, which **joint is typically involved in osteoarthritis?**

A: Distal interphalangeal joints (DIP).

Q: What are the diseases that involve **DIP?****A:** As follows:

- Osteoarthritis.
- Psoriatic arthritis.
- Gout.

Q: What are **clinical feature osteoarthritis? How to **investigate**?****A:** As follows:

Symptoms:

- Pain of the affected joints. Pain increases with activity and diminishes with rest. Commonly knee and hip joints are involved. Difficulty in walking, sitting, raising from sitting.
- Limitation of movement.

Signs:

- swollen with restricted movement. Later on joint deformity may occur.
- In hand—bony swelling at the proximal (Bouchard node) and distal (Heberden's node) interphalangeal joints. DIP joints are commonly involved.
- Crepitus on movement of the joints.

Investigation:

- X-ray of the affected joints: shows joint space narrowing, osteophyte and marginal sclerosis.

Q: How to treat osteoarthritis?

A: As follows:

- Explanation and reassurance.
- Patient's education.
- Regular exercise.
- Weight reduction if obese.
- Reduction of adverse mechanical factors.
- Use of appropriate footwear, walking stick etc.
- Pain relief—paracetamol, NSAID. Intra-articular corticosteroid may be needed.
- Chondroitin sulphate and glucosamine sulphate may be helpful.
- Intra-articular hyaluronic acid is also helpful.
- Physiotherapy should be given.
- Surgery in some cases: osteotomy and joint replacement

CHARCOT'S JOINT

Instruction by the examiner:

- Look at the patient's knee or ankle joint or examine the lower limbs.

Presentation of a Case:

- The right knee joint is swollen and deformed. Movement produces crepitus sounds.

My diagnosis is **Charcot's joint**.

Q: What are your **differential diagnoses**?

A: As follows:

- Osteoarthritis.
- Severe rheumatoid arthritis.
- Chronic gouty arthritis.

Q: What **else** do you like to see or what history do you like to take?

A: As follows:

- Sensory examination.
- In the upper limb: dissociated sensory loss (to exclude syringomyelia).
- History of lancinating pain, signs of posterior column lesion and Argyll Robertson pupil (to exclude tabes dorsalis).
- History of diabetes mellitus.



Charcot's joint of both elbow



Charcot's joint of both knee



Charcot's joint of both feet

Q: What is **Charcot's joint**? What are the **causes**? What are the **features** of Charcot's joint?

A: It is the complete destruction and disorganization of the joint, usually secondary to loss of proprioception of the joint sense. Causes are:

- Diabetes mellitus (usually involves the joint of foot). It is the commonest cause.
- Syringomyelia (usually involves joint of upper limbs: elbow, shoulder joint).
- Tabes dorsalis (usually involves joint of lower limbs: knee, ankle).
- Leprosy.
- Repeated intra-articular injection of steroid.
- Others: meningomyelocele, hereditary sensory neuropathy, peripheral nerve injury etc.

Features of Charcot joint:

- Painless joint with deformity.
- Enlargement of joint with bony outgrowth, subluxation and crepitus. Joint may be unstable.
- Joint effusion may occur.

Q: What are the x-ray findings?

A: As follows:

- Reduction, destruction and disorganization of the joint.
- Loose bodies.
- Marginal sclerosis.

Q: How to treat?

A: As follows:

- Treatment of primary cause,
- Orthopaedic measures.

EXAMINATION OF THE EYE

10

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EXAMINATION OF THE EYE

10

‘To all students of medicine—who listen, look, touch and reflect: may they hear, see, feel and comprehend.’
—Barlow

INTRODUCTION

Examination of eye or usually fundoscopy is an important topic in any clinical examination, mostly as short case. However in some long case such as diabetes mellitus or any neurological case, fundoscopy is usually necessary. Also while examining cranial nerve, eye is an important part. Very often, examiner asks, ‘Examine the fundus. What are your findings? Or, Examine the eye of this patient. Or, Look at the eyes. What are your findings? (May be ptosis, exophthalmos, squint, xanthelasma, arcus senilis, subconjunctival haemorrhage and heliotrope rash)’.

Proceed as follows: Before examining the eyes, the patient should sit at the edge of the bed facing the examiner.

Inspection:

1. Look at the face to see any facial asymmetry (in hemiplegia, Bell’s palsy), myasthenic, myotonic, tabetic face and thyrotoxic or hypothyroid face.
2. Ptosis (complete or partial), squint, exophthalmos, eyebrows (fall of lateral one-third or all), xanthelasma, lid retraction, puffy face with baggy eyelids and heliotrope rash.
3. Cornea (arcus, Kayser–Fleischer or KF ring, band keratopathy, ulceration, Bitot’s spot).
4. Sclera (blue sclera, pigmentation, redness, chemosis).
5. Pupil:
 - Size (dilatation or constriction).
 - Shape (irregular or unequal).
 - Light reflex (direct and consensual).
 - Accommodation reflex.
6. Movement of the eyeball:
 - Keep the head of the patient fixed. Tell the patient: ‘Follow my finger’.
 - See both horizontally and vertically like ‘H’.
 - During movement of eyes: Look for nystagmus, diplopia (by asking the patient to look at extreme gaze), lid lag and lid retraction.

7. Look for:

- Acuity of vision (for distant and near vision).
- Colour vision.
- Field of vision.
- Corneal reflex.

8. Finally, **perform** fundoscopy. Proceed as follows:

- The patient should be examined either in sitting or lying down in a dark room.
- Ask the patient to look straight and keep his or her eyes open.
- You should use your right or left eye to examine the patient's corresponding eye.
- Look at the eye from at least 50 cm and check for red reflex (start with 201 red numbers). Opacity in media of the eye (cornea, anterior chamber, lens and vitreous) will appear as black specks or lines against red reflex.
- Look at the following points by gradually coming from red numbers to black (negative) and ophthalmoscope brought close to the patient's eye:
 - Optic disc (comment on colour, margin and cup. Normal optic disc is rich in yellow colour, rest of fundus is rich in red colour).
 - Macula (one or two discs away from and a little below the temporal margin of the disc). It appears darker than the surrounding retina and in young individuals has a central yellow point called 'fovea centralis'.
 - See the nasal and temporal halves of fundus and then the whole fundus.
 - Look retinal vessels (retinal artery has 4 main branches and normal ratio of artery to vein is 2:3).
 - Look for transparency of vessels (arteries usually have a shiny central reflex stripe), presence of arteriovenous (AV) nipping and tortuosity of veins.
 - Look for exudate and haemorrhage.

Present your findings systematically.

OPTIC ATROPHY

Instructions by the examiner:

- Examine the fundus. What are your findings?

Presentation of a Case: Case No. 1 (Mention in Which Eye—Right or Left or Both).

- The disc is pale with clear margin.
- There is reduction of number of capillaries in the disc (normally 7 to 10 capillaries cross the disc margin).
- No other changes in retina.

My diagnosis is **Primary optic atrophy (OA)**.

Q: Why primary OA?

A: Because, the disc is pale with clear margin and no change in the retina.

Q: Why not secondary OA?

A: In secondary OA:

- Disc: greyish white.
- Margin: indistinct.
- Some changes in the retina are present (e.g., exudate or haemorrhage).

Q: What is the mechanism of primary OA?

A: Degeneration of optic nerve fibres.

Presentation of a Case: Case No. 2:

- The disc is greyish white with indistinct margin.
- There are few exudates and haemorrhage in the retina (mention the location).

My diagnosis is **Secondary OA**.

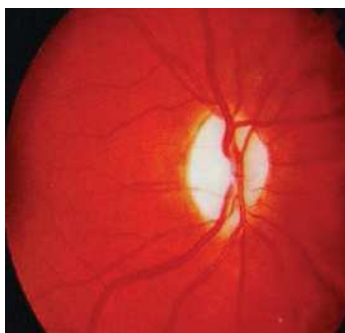
Q: Why secondary OA?

A: Because:

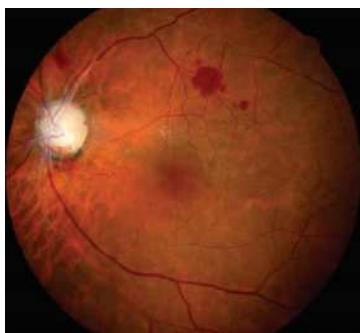
- Disc is greyish-white with indistinct margin.
- There is exudate and haemorrhage in the retina.

Q: What do you think is the cause of secondary OA?

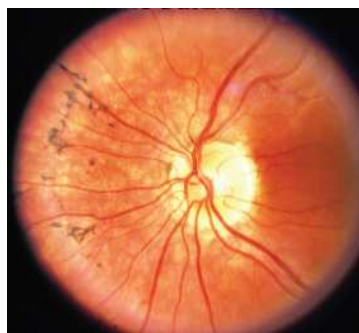
A: Secondary to papilloedema (usually long standing).



Primary optic atrophy



Secondary optic atrophy



Conjunctive optic atrophy

Q: What **relevants** do you want to see in optic atrophy?

A: I want to see:

- Light reflex: direct and consensual (in advanced OA, pupil reacts consensually but not directly).
- Visual Acuity: Mild to complete loss of vision may occur.
- Colour Vision: May be lost.
- Field of Vision (there is constriction or reduction of visual field in advanced stage). Central scotoma is found in optic neuritis.
- Features of multiple sclerosis (as it is the commonest cause of optic neuritis causing optic atrophy).

Q: What do you think are the **causes** optic atrophy in this patient?

A: As follows:

- Intracranial space occupying lesion (ICSOL).
- Secondary to optic neuritis (in multiple sclerosis).
- Glaucoma.
- Optic nerve compression (by tumour or aneurysm).

Q: How do you **investigate** in a case of OA?

A: As follows:

- CBC and PBF (there may be macrocytic anaemia due to vitamin B₁₂ deficiency).
- Serological test for syphilis (VDRL, TPHA).
- X-ray of the skull.
- CT scan or MRI of brain.
- Other investigations according to the suspicion of causes.

READ THE FOLLOWING TOPICS IN OPTIC ATROPHY

Q: What are the **types** of OA?

A: 3 types:

- Primary (due to optic neuritis, compression in the optic nerve, glaucoma).
- Secondary (to papilloedema).
- Consecutive (secondary to the disease of retina such as retinitis pigmentosa, chorioretinitis, Tay–Sach's disease).

N.B: The term consecutive is controversial. It is **actually** a secondary OA.

Q: What are the causes of primary OA?**A:** As follows:

1. Raised intracranial pressure due to intracranial SOL (neoplasm, abscess, cyst).
2. Secondary to optic neuritis, which may be due to:
 - Demyelinating disease (multiple sclerosis).
 - Drugs (ethambutol, quinine, chloroquine) and toxins (methyl alcohol poisoning, lead, arsenic, cyanide poisoning).
 - Neurosyphilis.
 - Nutritional amblyopia (vitamin B₁₂ deficiency, tobacco, alcohol).
3. Hereditary (Friedreich ataxia, Leber's OA, DIDMOAD syndrome).
4. Ischaemic optic neuropathy (in giant cell arteritis).
5. Others: Trauma to the optic nerve, Paget's disease, retinal artery occlusion.

Cause of secondary OA: It is due to long standing papilloedema.

Q: What is DIDMOAD syndrome?**A:** It is the combination of:

- **DI:** Diabetes insipidus.
- **DM:** Diabetes mellitus.
- **OA:** Optic atrophy.
- **D:** Deafness.

Q: What is glaucomatous OA?**A:** Glaucomatous OA denotes loss of disc substance. Cup is enlarged and emerging vessels appear to bend sharply outwards.**Q: What is the difference between optic neuritis and optic atrophy?****A:** Optic neuritis is an acute inflammatory process affecting the optic nerve. Optic atrophy is the degeneration of the optic nerve head, sometimes a sequel to optic neuritis.**Q: What is 'ischaemic optic neuropathy'?****A:** In this condition, there is infarction of anterior part of optic nerve resulting in acute severe loss of vision. Causes are:

- Temporal Arteritis (commonest).
- Others: Retinal artery occlusion, arteriosclerosis, severe hypotensive episodes.

PAPILLOEDEMA (PURE)

Instructions by the examiner:

- Examine the fundus. What are your findings?

Presentation of a Case: (Mention in Which Eye, Right or Left or Both)

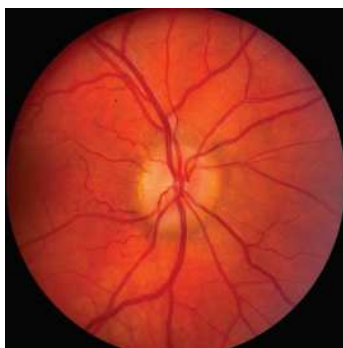
- There is bilateral papilloedema, more marked in right or left eye.
- No abnormality in retina.
- No abnormality of retinal vessels.

My diagnosis is **Bilateral Papilloedema**.

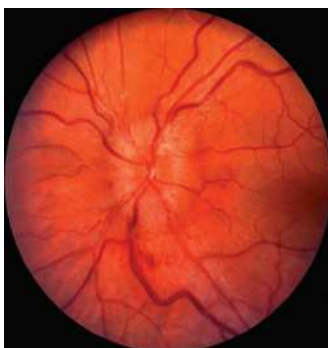
Q: What do you think the **cause** in this case?

A: Possible causes are (in the absence of exudate or haemorrhage or other changes in retina):

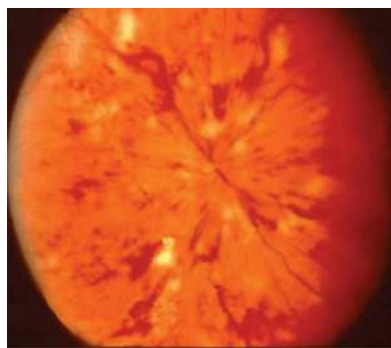
- Raised intracranial pressure due to ICSOL (neoplasm, abscess, haematoma).
- Benign or idiopathic intracranial hypertension.



Papilloedema (Left eye)



Papilloedema (Right eye)



Papilloedema with haemorrhage and exudates in fundus (malignant hypertension)

Q: Could it be **malignant hypertension**?

A: Unlikely, because in malignant hypertension, there will be other changes of hypertensive retinopathy, such as, AV nipping, exudate and flame shaped haemorrhage.

Q: Which disease is **confused** with papilloedema?

A: It is confused with:

- Papillitis (optic neuritis).
- Pseudopapilloedema.
- Drusen (hyaline bodies): Pale yellow spots, mostly in macula.
- Myelinated nerve fibres.

N.B. If confusion arises, it may be confirmed by fluorescence angiography. In papilloedema, leaking of dye in capillaries occur.

Q: What is **pseudopapilloedema**?

A: It is a developmental anomaly of optic nerve, there is no oedema. It has no clinical significance.

Q: What is the **visual abnormality** in papilloedema?

A: Transient obscurations of vision due to temporary impairment of retinal blood flow.

Q: What is the **field defect** in papilloedema?

A: Peripheral constriction of visual field and blind spot is enlarged.

Q: What is the important **sign** in papilloedema due to raised intracranial tension?

A: Absence of venous pulsation.

N.B: Remember the following points:

- Visual Acuity is usually preserved but may be affected in late stage.
- Blind spot is enlarged.

READ THE FOLLOWING TOPICS IN PAPILLOEDEMA

Q: What is **papilloedema**? What are the **stages** of papilloedema?

A: It is the swelling of the optic nerve head. Stages are:

- Early sign: Absence of spontaneous pulsation of retinal veins and increased pink or red colouration of the disc.
- Blurring of disc margin, first starting in nasal side.
- Filling of physiological cup.
- Fullness of optic disc, then elevation.
- Vessels on the disc become curved over its edge.
- May be haemorrhage surrounding the disc.

Q: What is **papillitis**?

A: It is the inflammation of optic nerve head is called papillitis or intraocular optic neuritis.

Q: What is **retrobulbar optic neuritis**?

A: Inflammation of the orbital or posterior portion of optic nerve is called retrobulbar optic neuritis or orbital optic neuritis. No ophthalmological change on fundoscopy.

Q: What are the **differences** between papillitis (optic neuritis) and papilloedema?

A: As follows:

Features	Papillitis (Optic Neuritis)	Papilloedema
1. Eye	Painful, specially on movement	No pain
2. Visual acuity	Markedly reduced	Slightly reduced in advanced cases
3. Colour vision	Affected (red)	Normal
4. Central scotoma	Present	Absent, there is peripheral constriction of visual field
5. Blind spot	Normal	Increased
6. Pupil	Dilated, less reaction to bright light	Normal

Q: What are the causes of papilloedema?**A:** As follows:

1. Raised intracranial pressure due to any cause (such as ICSOL, intracranial haemorrhage, venous sinus thrombosis, cerebral oedema, hydrocephalus, meningitis, encephalitis).
2. Hypertensive retinopathy (in malignant hypertension).
3. Benign or idiopathic intracranial hypertension.
4. Central retinal vein occlusion.
5. Others:
 - CO₂ retention (hypercapnia).
 - Subarachnoid haemorrhage or cerebrovascular disease (CVD).
 - Secondaries in brain.
 - Guillain–Barré syndrome.
 - Graves' disease.
 - Cavernous sinus thrombosis.
 - Severe anaemia.
 - Hypoparathyroidism or hypocalcaemia.
 - Hypervitaminosis A.

Q: What are the causes of unilateral papilloedema?**A:** As follows:

- Central retinal vein occlusion.
- Foster Kennedy syndrome.
- Infiltration in one eye (lymphoma, leukaemia and sarcoidosis).
- Early stage of bilateral papilloedema.

Q: What is Foster–Kennedy syndrome?**A:** It is characterized by a frontal lobe tumour compressing optic nerve causing ipsilateral optic atrophy but contralateral papilloedema due to raised intracranial pressure.**Q: What is benign or idiopathic intracranial hypertension (BIH)? What are the causes?****A:** It is a syndrome of raised intracranial tension in the absence of intracranial SOL or ventricular dilatation or focal neurological signs. Actual cause is unknown. There is reduction of reabsorption of CSF by arachnoid villi. Common in females, 18 to 40 years of age, obese and rarely familial. Predisposing factors are:

- Drugs: Tetracycline, nalidixic acid, oral contraceptive pill, Hypervitaminosis A, nitrofurantoin, sulphur drugs, phenytoin, steroid (both therapy and withdrawal).
- Endocrine disorders: Hyperthyroidism, hypothyroidism, hypoparathyroidism, Addison's disease, Cushing's syndrome.
- Obesity.
- Pregnancy, menarche, puerperium.
- Collagen disease: SLE, cryoglobulinaemia.
- Others: middle ear disease, dural sinus thrombosis or obstruction, head injury.

Q: What is the commonest presentation of BIH?**A:** Frequent headache, also visual disturbance.

Q: What is the **complication** of BIH?

A: Visual loss.

Q: What are the **physical finding** in primary optic atrophy?

A: Only papilloedema in fundoscopy. Features of primary disease may be present.

Q: How to **diagnose** BIH? What **investigations** do you suggest?

A: Diagnosis is done by exclusion of other diseases. Investigations are:

- X-ray of skull (may be increased size of sella turcica).
- Lumbar puncture shows increased CSF pressure and no other changes in CSF.
- CT or MRI of brain (to exclude other pathology).
- Sometimes MR angiography or cerebral venography may be done to exclude cerebral venous sinus thrombosis.

Q: How to **treat** BIH?

A: As follows:

1. Treatment of predisposing factors (reduce obesity and avoid precipitating drug).
2. Frusemide or acetazolamide, steroid may be given.
3. Frequent lumbar puncture (may be done on alternate days).
4. If no response, Surgical treatment:
 - Lumbo-peritoneal shunt or ventriculo-peritoneal shunt, especially if progressive visual loss.
 - Optic nerve sheath fenestration may be done.

RETINAL VEIN OCCLUSION (CENTRAL AND BRANCH RETINAL VEIN OCCLUSION)

Instructions by the examiner:

- Examine the fundus. What are your findings?

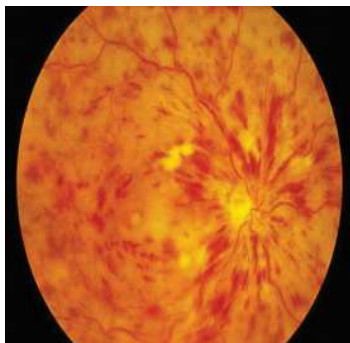
Presentation of Case No. 1: (Mention in Which Eye, Right or Left)

- There are multiple scattered haemorrhages over the whole retina, some are flame shaped.
- The veins are dilated and tortuous.
- Few soft exudates are present
- There is bilateal papilloedema are present.

My diagnosis is **Central retinal vein occlusion (CRVO)**.

Q: What is the **appearance** of haemorrhage in CRVO?

A: Stormy sunset appearance (or blood and thunder appearance).



Central retinal vein occlusion
(bleeding with multiple exudate)



Central retinal vein occlusion (more
severe—with multiple bleeding)



Branched retinal vein occlusion

Q: What are the **causes** of CRVO?

A: As follows:

- Hypertension (common, 70% cases).
- Atherosclerosis.
- Diabetes mellitus.
- Hyperviscosity syndrome (causes are multiple myeloma, Waldenström's macroglobulinaemia, polycythaemia rubra vera).
- SLE.
- Others: Leukaemia, hyperlipidaemia, nephrotic syndrome, antiphospholipid syndrome, hypercoagulable state (antithrombin III deficiency, protein S or C deficiency, factor V Leiden mutation) etc.

Q: What is the **prognosis** of CRVO?

A: As follows:

- In mild case without macular involvement: there is no visual disturbance.
- In severe case: there is marked visual deterioration. Secondary glaucoma may occur due to new vessels formation.

Q: What are the **complications** of CRVO?

A: As follows:

- Neovascularization of retina (may require laser therapy).
- Rubeosis iridis.
- Glaucoma (rubeotic).
- Optic atrophy.
- Permanent loss of vision.
- Traction retinal detachment.

Q: What is the **relation** of glaucoma with retinal vein occlusion?

A: Retinal vein occlusion is 5 times more in glaucoma than non-glaucoma patients.

Q: What **investigations** should be done in central retinal vein occlusion?

A: As follows:

- CBC with ESR (polycythaemia may be present).
- Blood sugar.
- Bone marrow (to exclude multiple myeloma).
- Plasma viscosity.
- Plasma protein electrophoresis.
- Lipid profile.
- Other investigations according to suspicion of causes.

Q: How to **treat**?

A: As follows:

- Treatment of primary cause.
- Referred to Ophthalmologist (panretinal photocoagulation, PRP by laser therapy. Anti-VEGF injections may be considered).

Presentation of Case No. 2: (Mention in Which Eye, Right or Left or Both).

- There are multiple scattered haemorrhages over the right lower part of the retina.
- The veins are dilated and tortuous.
- Few soft exudates are present.

My diagnosis is **Branch retinal vein occlusion**.

Q: What is the **prognosis** in **branch retinal vein occlusion**?

A: Prognosis is good, if haemorrhage does not involve macula.

N.B. Superior temporal vein is commonly involved. There may be quadrantic field defect in such case.

HYPERTENSIVE RETINOPATHY

Instructions by the examiner:

- Examine the fundus. What are your findings?

Presentation of Case No. 1: (Mention in Which Eye, Right or Left).

- Retinal arterioles are irregular, tortuous and narrow.
- There is silver wiring with increased light reflex.
- Veins are engorged, arterio-venous nipping is present.
- There are flame shaped haemorrhages in upper temporal region.
- Few cotton-wool spots and few hard exudates are present in quadrants.
- If hard exudate occurs around macula or fovea, it is called **macular star** (mention, if any).

My diagnosis is **Hypertensive retinopathy (grade 3)**.

Q: Why **not** this is diabetic retinopathy?

A: In diabetic retinopathy:

- Haemorrhage: usually dot and blot.
- No AV nipping.
- Hard exudates (usually).

Presentation of Case No. 2:

- Present as in case 1 **plus**
- There is bilateral papilloedema.

My diagnosis is **Hypertensive retinopathy (or grade 4, may be malignant hypertension)**.

Q: What are the **causes** of AV nipping?

A: As follows:

- Hypertensive retinopathy (grade II).
- Atherosclerosis.



Flame-shaped haemorrhage, cotton wool spot



Flame-shaped haemorrhage, cotton wool spot, papilloedema, AV nipping



Papilloedema, macular star

Q: What is cotton-wool spot and what are the causes?

A: It indicates area of retinal infarction or ischaemia. Causes are:

- Hypertension.
- Occasionally diabetes mellitus.
- Central retinal vein occlusion.
- Central retinal artery occlusion.
- Severe anaemia.
- SLE (called cytoid body).
- Others: leukaemia, infective endocarditis (Roth spot), HIV infection.

Q: What is malignant hypertension? What does it indicate?

A: It is characterized by severe hypertension with diastolic BP >130 mmHg, associated with grade III or IV retinopathy (retinal haemorrhage or exudates and papilloedema) and renal failure or encephalopathy. If untreated, death occurs within months.

Q: What is the pathogenesis of malignant hypertension?

A: Unknown, probable mechanisms are:

- Fibrinoid necrosis of the wall of small artery and arteriole, which results in end organ damage.
- Dilatation of cerebral arterioles (due to auto-regulation), which may result in cerebral infarction or haemorrhage.

Q: What are the complications of malignant hypertension?

A: Blindness, renal failure, even death may occur.

Q: How to treat?

A: Slow, controlled reduction of BP over a period of 24 to 48 hours is ideal (rapid reduction is avoided as it reduces tissue perfusion and can cause cerebral damage including occipital blindness, may even precipitate coronary or renal insufficiency).

- Complete rest.
- Sedation, if needed.
- Oral antihypertensive is sufficient to control BP. Sublingual nifedipine may be given.
- Sometimes IV or IM labetalol, IV glycerine trinitrate, IM hydralazine.

Q: What are the grades of hypertensive retinopathy?

A: 4 grades (Keith–Wagener–Barker classification):

- **Grade I:** Thickening of arterial wall, increase tortuosity, narrowing of arteriole and increased light reflex (silver wiring).
- **Grade II:** Grade I plus AV nipping and reduction of arterial calibre in comparison to vein (normal ratio of V:A = 3:2).
- **Grade III:** Grade II plus cotton-wool exudate and flame-shaped haemorrhage.
- **Grade IV:** Grade III plus papilloedema (Grades III and IV indicate malignant hypertension).

Q: What are the ocular complications of hypertension?

A: Hypertensive retinopathy, retinal vein occlusion.

RETINAL HAEMORRHAGE

Instructions by the examiner:

- Examine the fundus. What are your findings?

Presentation of the Case:

- There are few haemorrhages (mention the location), some are flame shaped and some are irregular in outline.
- The fundus looks pale, disk is normal.

My diagnosis **Multiple haemorrhage** (right or left or both).

Q: What are the **causes** of retinal haemorrhage in this case?

A: As follows:

- Aplastic anaemia.
- Thrombocytopenia.
- Leukaemia.
- Haemophilia.
- Christmas disease.
- Severe anaemia due to any cause.
- Anticoagulant drug therapy.

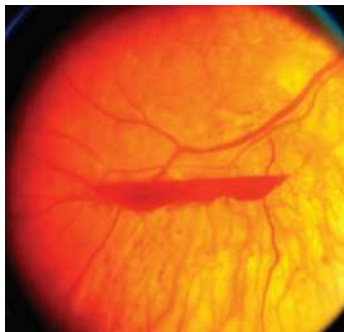
Q: What are the **other causes** of retinal haemorrhage?

A: As follows:

- Hypertension.
- Diabetes mellitus.
- Atherosclerosis.
- CRVO due to any cause.
- Subarachnoid haemorrhage (subhyaloid with crescentic-shaped or straight horizontal border).
- Raised intracranial pressure due to any cause.



Retinal haemorrhage



Preretinal haemorrhage



Roth's spot with haemorrhage

Q: How to **treat** retinal haemorrhage?

A: Treatment of underlying cause.

Q: What is **Roth spot**? What are the **causes**?

A: Retinal haemorrhage with a white spot in the centre is called Roth spot. Causes are:

- Infective endocarditis (due to autoimmune vasculitis).
- Leukaemia.
- SLE.
- Severe anaemia.

DIABETIC RETINOPATHY

Instructions by the examiner:

- Examine the fundus. What are your findings?

Presentation of Case No. 1: (Mention in Which Eye, Right or Left.)

- There are microaneurysm of capillaries (mention the location).
- Few haemorrhages (dot and blot), which are small and round shaped.
- Also there are hard exudates (yellowish with clear margin).
- Disc is normal.

My diagnosis is **Diabetic retinopathy**, simple background.

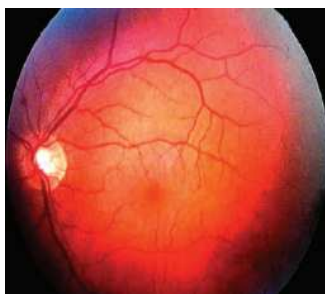
Q: Why this is **not** hypertensive retinopathy?

A: In hypertensive retinopathy, there will be:

- AV nipping.
- Soft or cotton-wool exudate.
- Flame-shaped haemorrhage.

Q: In simple background retinopathy, what are the **symptoms** of the patient?

A: Usually asymptomatic, as the macula is spared.



Dot haemorrhage and microaneurysm



Dot and blot haemorrhage (soft exudate)



Dot and blot haemorrhage (hard exudate)

Q: What is microaneurysm? What are the **causes of microaneurysm** of capillaries?

A: Microaneurysms are the out pouching of capillary walls due to pericyte loss, appears as small red dots. It is the early sign of diabetic retinopathy. Causes are:

- Diabetes mellitus (common).
- Hypertension (usually in malignant hypertension).
- Atherosclerosis.
- Collagen diseases (SLE, polyarteritis nodosa).
- Others: sickle cell anaemia, leukaemia, mycotic aneurysm, retinal vein occlusion.

N.B. Microaneurysm is always along the vessel wall, it may be confused with haemorrhage. Confirmed by fluorescence angiography.

Q: Why haemorrhage?

A: It is due to rupture of microaneurysm, resulting in dot and blot haemorrhage.

Q: What are hard exudates?

A: These are lipid and protein residues of serous leakage from the vessels, yellowish in colour and irregular in outline with sharply defined margin.

Q: How to treat such a case?

A: As follows:

- Control of diabetes mellitus, stop smoking and control of hypertension (if any).
- Annual fundal examination.
- For leaking microaneurysm: Argon laser photocoagulation may be done.

N.B. Simple retinopathy is rare in young, if DM <10 years duration, but common if >20 years duration. In older patient with diabetes mellitus, early development may occur.

Presentation of a Case (Maculopathy): Case No. 2:

- Findings as in case 1 **plus**
- Haemorrhage and hard exudates encroaching upon the macula (maculopathy or macular oedema).

My diagnosis is **Background diabetic retinopathy with maculopathy**.

Q: What are the symptoms of the patient?

A: Visual impairment, mainly central vision (reduction of visual acuity). Diabetic maculopathy is one of the common causes of loss of vision in patient with non-proliferative retinopathy.

Q: In which diabetes it is common?

A: It is common in the elderly in NIDDM.



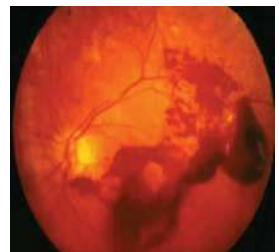
Maculopathy



Preproliferative retinopathy



Proliferative retinopathy



Proliferative retinopathy
(Severe vitreous haemorrhage)

Q: How to treat such a case?

A: As follows:

- Good control of diabetes mellitus.
- Photocoagulation may improve visual acuity in 50% cases.

Presentation of Case No. 3 (Mention in Which Eye, Right or Left):

- As in case no. 2 **plus**
- Multiple large blot haemorrhages and cotton-wool spots.
- Venous dilatation, venous beading and venous loops are also present.

My diagnosis is **Pre-proliferative diabetic retinopathy**.

Q: What are the features of **pre-proliferative** retinopathy?

A: As follows:

- Multiple cotton-wool spots (earliest sign).
- Venous abnormality (irregular, beading, reduplication and loops).
- Multiple haemorrhage and intra-retinal microvascular abnormality.

Q: How to **treat** pre-proliferative retinopathy?

A: As follows:

- Good control of DM.
- Photocoagulation in some cases.
- Regular follow up should be done.

Presentation of a Case (Proliferative Type): Case No. 4:

- Findings as in case no. 3 **plus**
- Venous dilatation, tortuosity and beading.
- There are some new vessel formations around the disc and few vitreous haemorrhage.

My diagnosis is **Proliferative diabetic retinopathy**.

Q: What are the features of **proliferative** retinopathy?

A: As follows:

- Exudative maculopathy.
- Pre-retinal haemorrhage.
- New vessels formation and fibrous proliferation.

Q: What are the **symptoms** of the patient in proliferative retinopathy?

A: As follows:

- Asymptomatic without macular involvement.
- Blurring of vision with macular involvement.

Q: What are the **treatment** of proliferative retinopathy?

A: As follows:

- Good control of DM.
- Photocoagulation.

Q: What is the **prognosis**?

A: Prognosis of proliferative retinopathy is variable if untreated. 50% may develop blindness within 5 years.

Presentation of Case No. 5:

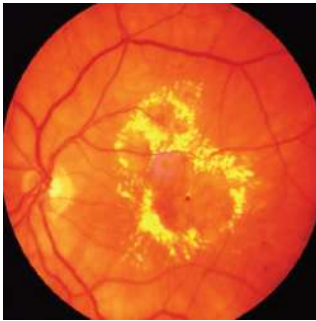
- As in case no. 4. **Plus**
- There are multiple photocoagulation scars (appears like exudate, with areas of small brown or yellowish spot of variable size and shape).

My diagnosis is **Proliferative diabetic retinopathy, treated with photocoagulation.**

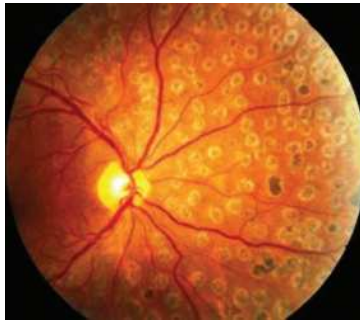
Q: What are the **complications** of proliferative retinopathy?

A: As follows:

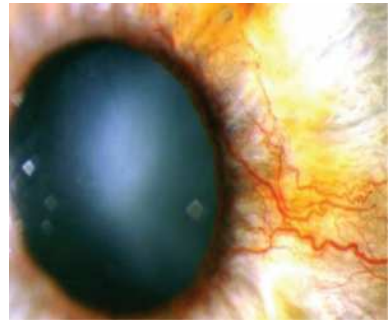
- Vitreous haemorrhage.
- Retinal detachment.
- Glaucoma (rubeotic glaucoma).
- Rubeosis iridis (new vessel formation in iris).



Macular photocoagulation



Pan-retinal photocoagulation



Rubeosis iridis

Q: In which **type of DM**, proliferative retinopathy is more common?

A: It is common in IDDM of long duration.

N.B. Remember the following points of retinopathy in DM:

- The overall prevalence is 25%. It occurs in 40% cases of IDDM and 20% of NIDDM.
- Depends on the duration of DM.
- If DM occurs before 30 years, the incidence of retinopathy is 50% after 10 years and 90% after 30 years.
- It is unusual for retinopathy to develop within 5 years of the onset of DM. However, 5% patients with NIDDM have background retinopathy at presentation.

Q: What are the **causes of retinal neovascularization**?

A: As follows:

- DM.
- Rarely malignant hypertension, sickle cell anaemia, sarcoidosis, hyperviscosity syndrome and Behcet's syndrome.

Q: What is the **pathogenesis** of new vessel formation?

A: Unknown, probably there is production of angiogenic factors from the area of ischaemic retina. Recently, a substance called 'vascular endothelial growth factor' (VEGF) has been isolated from ocular fluid, which is angiogenic.

These new vessels are very fragile and leaking, liable to rupture causing haemorrhage (intraretinal, preretinal or vitreous). Serous protein leakage from these vessels stimulates connective tissue reaction called retinitis proliferans. Later on, retinal detachment may occur.

READ THE FOLLOWING TOPICS IN RELATION TO DIABETIC OCULAR COMPLICATION

Q: What are the **eye problems** in diabetes mellitus?

A: As follows:

- Diabetic retinopathy.
- Cataract.
- Central retinal vein occlusion.
- Glaucoma.
- Rubeosis iridis.
- Retinal artery occlusion.

Q: What is the cause of **visual loss** in diabetes mellitus?

A: As follows:

- Macular oedema.
- Proliferative retinopathy.
- Retinal detachment.

Q: What are the **indications** of laser photocoagulation therapy in diabetic retinopathy?

A: As follows:

- Macular oedema.
- Preproliferative.
- Proliferative retinopathy.

Q: What are the **complications** of laser photocoagulation therapy?

A: As follows:

- Vitreous haemorrhage.
- Retinal vein occlusion.
- Constriction of visual field.
- Headache.

RETINITIS PIGMENTOSA

Instructions by the examiner:

- Examine the fundus. What are your findings?

Presentation of a Case:

- There are multiple areas of black pigmentation like bone spicules with variable size and shape, some in criss-cross pattern, at the periphery of fundus.
- Macula is normal and the disc is also normal. No exudate or haemorrhage.

My diagnosis is **Retinitis pigmentosa**.

Q: What else do you like to examine?

A: Visual field (which is constricted).

Q: What is your differential diagnosis?

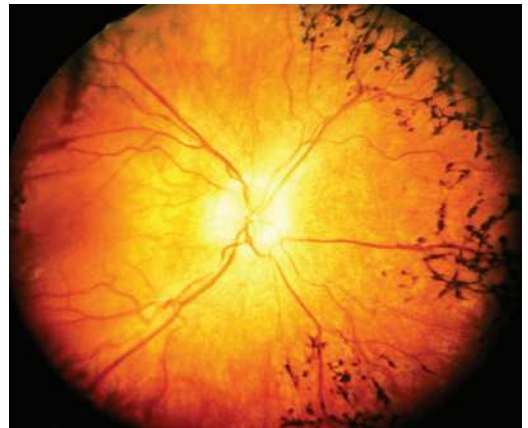
A: As follows:

- Old choroido-retinitis.
- Lesser photocoagulation scar.

Q: What is retinitis pigmentosa? What are the features?

A: It is a progressive degenerative disease of retina with pigmentary epithelium in a bone spicule pattern.

- It starts in early childhood and affects both eyes.
- Inherited as X-linked, autosomal recessive or autosomal dominant.
- May occur sporadically as an isolated ocular disorder and also associated with other disease.
- Degeneration primarily affects the rods and may also involve cones.
- Loss of vision by middle or advanced age. Visual acuity is normal initially, the patient is blind by 20 to 30 years.
- There may be constriction of peripheral field of vision and optic atrophy may occur (consecutive).
- Cataract is a common complication causing further visual impairment.
- Rod are responsible with vision in starlight or moonlight, cone photoreceptors are important for colour vision and fine acuity in daylight. Rods are mainly affected, causing night blindness and loss of peripheral vision.



Q: What are the causes of retinitis pigmentosa?

A: As follows:

- Isolated or congenital: Bardet–Biedl syndrome (previously called Laurence–Moon–Biedl syndrome).
- Hereditary ataxia (e.g., Friedreich’s ataxia).
- Refsum’s disease.
- Abetalipoproteinaemia.
- Usher’s disease.
- Alström’s syndrome.
- Familial neuropathies.

Q: What is the **common complaint or presentation** of retinitis pigmentosa?

A: Night blindness (due to reduction of rods at the periphery of retina).

Q: What are the **visual symptoms associated with** retinitis pigmentosa?

A: As follows:

- Night blindness.
- Loss of peripheral vision (tunnel vision).
- Photopsia (flashes of light).
- Impairment of vision (due to consecutive optic atrophy).

Q: What is the **best diagnostic test** for retinitis pigmentosa?

A: Electroretinogram (ERG). It provides objective measure of rods cones function.

Q: How to **treat**?

A: As follows:

- Regular and periodic check up.
- Treatment of primary cause, if any.

PTOSIS

Instructions by the examiner:

- Look at the face. What is your findings? What else do you want to see? Or, Examine the eyes.

(If obvious ptosis, is it bilateral or unilateral, complete or partial? Ask the patient to open the eyes, the patient is unable).

Presentation of a Case (Unilateral Ptosis in IIIrd Nerve Palsy): Case No. 1: (By Looking at the Face)

- There is complete ptosis in the right (or the left) side.

My diagnosis is **Complete ptosis due to IIIrd nerve palsy**.

Q: What else do you want to see?

A: As follows: raise the upper eye lid, see the following—

- Divergent squint (eyeball is fixed in downward and outward position).
- Pupil (dilated and fixed, no reaction to direct and consensual light).
- No movement of eyeball in upwards, downwards and medially.
- Loss of accommodation.
- May be diplopia (angulated, mention in which direction).



Unilateral ptosis IIIrd nerve palsy (left)



Right-sided IIIrd nerve palsy (dilated pupil)



Bilateral partial ptosis (Horner's syndrome)

Q: What are the causes of unilateral ptosis?

A: As follows:

- Congenital.
- Traumatic.
- Senility.
- Complete IIIrd nerve palsy.
- Horner's syndrome (there is partial ptosis).
- Myasthenia gravis (may cause unilateral or bilateral ptosis).
- Hysterical conversion reaction.

N.B. Sometimes, IIIrd nerve palsy may be partial, pupil may be spared. Found in diabetes mellitus and vasculitis, which causes infarction of the nerve. Parasympathetic fibres supplying the pupil remain intact and spare the pupil.

Q: Why **ptosis** and **dilated pupil** in the IIIrd nerve palsy?

A: As follows:

- Ptosis is due to paralysis of levator palpebrae superioris (supplied by IIIrd nerve).
- Dilated pupil is due to paralysis of constrictor of pupil (supplied by IIIrd nerve).

N.B.: Dilator of pupil is supplied by sympathetic nerve, which when paralysed, pupil is constricted as in Horner's syndrome.

Q: What are the **signs of IIIrd nerve lesion**?

A: As follows:

- Ptosis (complete).
- External squint.
- Pupil: Dilated, no reaction to direct and consensual light.
- Inability to move the eye upwards, downwards and medially.
- Loss of accommodation reflex.

Q: What are the **causes of IIIrd nerve lesion**?

A: As follows:

1. Nuclear lesion (causes are: infarction, haemorrhage, neoplasm and multiple sclerosis).
2. Midbrain with CVD (Weber's syndrome, in which there is ipsilateral IIIrd nerve palsy with contralateral hemiplegia due to thrombosis of a branch of posterior cerebral artery).
3. Unruptured aneurysm of posterior communicating artery (there is painful ophthalmoplegia).
4. Others:
 - Mononeuritis multiplex (due to DM, SLE, PAN, sarcoidosis, amyloidosis, leprosy).
 - Subacute meningitis (due to carcinoma, lymphoma, fungal, tuberculous, meningovascular syphilis).
 - Raised intracranial pressure (because the nerve has long and tortuous course, so likely to be compressed by any displacement of brain stem).
 - Ophthalmoplegic migraine.
 - Guillain-Barré syndrome.

Q: What **investigations** should be done in IIIrd nerve palsy?

A: As follows:

- CBC with ESR (high in vasculitis).
- Blood sugar.
- CT scan or MRI of brain.
- Occasionally, cerebral arteriography (if aneurysm is suspected).

Presentation of a Case (Bilateral Ptosis): Case No. 2: (By Examining the Eye).

- There is bilateral ptosis.
- Eye movement is normal in all directions.
- Pupil: Normal in size and shape, reacts to direct and consensual light.
- Accommodation is normal.
- (There is frontal baldness, wasting of temporalis and myotonia in myotonia dystrophica, mention if any).

My diagnosis is **Bilateral ptosis**.

Q: What are the causes of bilateral ptosis?**A:** As follows:

- Myasthenia gravis.
- Tabes dorsalis (there is bilateral ptosis with frontalis overaction, Argyll Robertson pupil, optic atrophy and dorsal column lesion).
- Myopathy (such as myotonia dystrophica and facio-scapulo-humeral myopathy).
- Ocular and oculo-pharyngeal myopathy.
- Bilateral Horner's syndrome (rare, may occur in syringomyelia).
- Congenital (rare).



Bilateral ptosis
(congenital)



Bilateral ptosis
(myasthenia gravis)



Bilateral ptosis (senile)



Bilateral ptosis
(ocular myopathy)

Q: How to differentiate between ptosis of myopathy and ptosis due to other cause?**A:** As follows:

- In patient with myopathy: there is no wrinkling of forehead.
- In other cases: there is overaction of frontalis with wrinkling of forehead.

Presentation of a Case (Ocular Myopathy): Case No. 3:

- There is bilateral ptosis, equal on both eyes.
- No compensatory wrinkling of forehead (may be wasting of muscles of face and neck).
- No movement of eyeball in any direction (complete ophthalmoplegia).
- Pupil is normal in size and shape, reacts to direct and consensual light.
- Accommodation is normal.

My diagnosis is **Ocular Myopathy or Oculo-pharyngeal myopathy**.

Q: Ask one question to this patient.

A: Any dysphagia. If present, then the diagnosis is **oculo-pharyngeal myopathy**.

Q: What is ocular myopathy?

A: It is a hereditary disorder, inherited as autosomal dominant or sporadic, common in young, characterized by bilateral ptosis with complete ophthalmoplegia. It may be due to absence of soft tissue in eyelid and periorbital region. Also there are mild facial and neck weakness.

Q: What is oculo-pharyngeal myopathy?

A: Like ocular, but associated with dysphagia due to cricopharyngeal achalasia. It is common in the elderly.

Presentation of a Case (Myotonic Dystrophy): Case No. 4:

- There is bilateral ptosis with frontal baldness, wasting of temporalis, masseter and sternomastoid.
- Face is long, lean, sad and expressionless.

My diagnosis is **Myotonia dystrophica** (see page 704).

N.B. During examination for ptosis, remember the following points:

- *If complete ptosis with divergent squint and dilated pupil: likely diagnosis is IIIrd nerve palsy.*
- *Partial ptosis with apparent enophthalmos and constricted pupil: likely diagnosis is Horner's syndrome.*
- *Absence of movement of eye ball in any direction: likely diagnosis is ocular or oculopharyngeal myopathy.*
- *If there is frontal baldness and temporal wasting: likely diagnosis is myotonic dystrophy.*
- *Bilateral ptosis with no movement of eyeball in any direction: likely diagnosis is ocular or occulo-pharyngeal myopathy.*

HORNER'S SYNDROME

Instructions by the examiner

- Examine the eye of this patient.
- Look at the eyes. What are your findings?

Presentation of a Case (Horner's Syndrome): Case No. 1: (Mention in Which Eye).

- There is partial ptosis with enophthalmos (eyeball looks shrunken and inwards). Ptosis can be overcome by voluntary upgaze.
- Pupil is constricted (miosis), reacts to both direct and consensual light.
- Movement of the eyeball is normal in all direction.
- There may be scar mark, lymphadenopathy, thyromegaly in the neck (mention if any).

My diagnosis is **Horner's syndrome** (right or left sided).

Q: What else do you want to see in this patient?

A: As follows:

- Neck: Lymph nodes, scar, thyromegaly, aneurysm (carotid and aortic).
- Chest: Apical lung signs (Pancoast's tumour).
- Hands: Clubbing, nicotine stain, wasting of small muscles of hands and pain.
- Evidence of syringomyelia (there will be dissociated sensory loss).
- Evidence of lateral medullary syndrome.
- Absence of sweating (on affected side of face, whole upper limb and upper part of trunk).



Horner's syndrome (left)



Horner's syndrome (bilateral)

Q: What is Horner's syndrome?

A: It is a syndrome due to lesion in the sympathetic pathway characterized by:

- Partial ptosis.
- Miosis (pupillary constriction), reacts to direct and consensual light.
- Enophthalmos (apparent).
- Anhidrosis (absence of sweating in affected side of face, whole upper limb and upper part of trunk).

Q: Why partial ptosis, miosis and enophthalmos in Horner's syndrome?

A: As follows:

- Partial ptosis is due to paralysis of upper tarsal muscles.
- Miosis is due to paralysis of dilator of pupil.
- Enophthalmos is due to paralysis of Muller's muscle.

Q: Why **not** complete ptosis?

A: Upper eye lid is controlled by Levator palpebrae superioris which is supplied by 3rd nerve.

Presentation of a Case (Horner's Syndrome): Case No. 2: (Bilateral)

- There is partial ptosis with enophthalmos in both eyes (eyeballs look shrunken and inwards).
- Ptosis can be overcome by voluntary upgaze.
- Both pupils are constricted (miosis), react to both direct and consensual light.
- Movement of both eyeballs are normal in all directions.

My diagnosis is **Bilateral Horner's syndrome**.

Q: What are the **causes** of Horner's syndrome (according to the site of lesion)?

A: As follows:

1. T₁ lesion:
 - Pancoast's tumour.
 - Trauma to brachial plexus.
 - Cervical rib.
2. Neck (sympathetic lesion):
 - Trauma.
 - Neck surgery.
 - Cervical sympathectomy.
 - Lymphoma.
 - Thyroid carcinoma.
3. Brain stem lesion:
 - Vascular (lateral medullary syndrome).
 - Multiple sclerosis.
4. Cervical cord lesion (bilateral Horner's syndrome may occur):
 - Syringomyelia.
 - Spinal cord tumour (glioma and ependymoma).
5. Migraine (temporary Horner's syndrome may occur).

Q: What **investigations** should be done in Horner's syndrome?

A: As follows:

- Chest x-ray.
- X-ray of cervical spine.
- CT scan or MRI of brain.
- Other investigations, according to suspicion of causes.

Q: Discuss the **cervical sympathetic pathway**.

A: It originates from the sympathetic nucleus in hypothalamus and passes through the brain stem to the lateral horn of C₈ and T₁ segment of spinal cord. From there, pre-ganglionic fibres emerge and pass to sympathetic ganglia (usually superior cervical ganglia). Then the post-ganglionic fibres pass in the carotid sheath with internal carotid artery, enter into the skull along with it and in the cavernous sinus, then join with the ophthalmic division of Vth nerve. Then it enters into the orbit via short ciliary nerve and supply the dilator pupillae, Muller's muscle and sweat glands on the side of face.

ARGYLL ROBERTSON PUPIL (AR PUPIL)

Instructions by the examiner:

- Examine the eye of this patient.

Presentation of a Case: (AR Pupil is Always Bilateral)

- Both the pupils are irregular, small and unequal.
- There is loss of light reflex (both direct and consensual), but accommodation reflex is normal.
- Iris shows patchy atrophy and depigmentation.
- Movement of the eyeball is normal in all direction.

My diagnosis is **AR pupil**.

Q: What are the **causes** of AR pupil?

A: As follows:

- Neurosyphilis (common cause) e.g., tabes dorsalis, general paralysis of insane (GPI).
- Diabetes Mellitus.

Q: What are the **features** of AR pupil?

A: AR pupil is characterized by—

- Pupil is small, irregular and unequal.
- Loss of light reflex, but persistence of accommodation reflex.
- Impaired response to mydriatic drug.
- Iris shows patchy atrophy and depigmentation.



AR pupil

Q: What is **site of lesion** of AR pupil?

A: Tectum of midbrain proximal to oculomotor nucleus, around aqueduct of sylvius.

Q: The patient has AR pupil. What **else** do you want to see?

A: I want to see the features of tabes dorsalis, such as—

- Wrinkling of forehead with bilateral ptosis (due to compensatory overaction of frontalis).
- Flaccid paraplegia.
- Loss of knee and ankle jerks, plantar is flexor (but in taboparesis, may be extensor).
- Posterior column lesion (such as loss of vibration and position sense).
- Loss of deep pain in Achilles tendon.
- Hypotonia.
- Bladder sensation is lost (there may be urinary retention and overflow incontinence).
- Gait may be stamping or steppage gait.
- Romberg sign is positive.
- Charcot joints may be present (commonly knee joint).
- Fundoscopy shows optic atrophy.

Q: What is the **lesion in heart linked** with AR pupil?

A: Aortic regurgitation.

Q: What are the **differences** between AR pupil and Holmes–Adie pupil?

A: As follows:

AR Pupil	Holmes–Adie Pupil
1. Bilateral	Usually unilateral
2. Pupil: small, irregular and unequal	Large, regular, one pupil is dilated
3. Loss of light reflex, but persistence of accommodation reflex	Slow reaction to light and accommodation
4. Impaired response to mydriatic	Normal response to mydriatic
5. Found in neurosyphilis	Unknown cause (benign condition)

HOLMES–ADIE PUPIL (MYOTONIC PUPIL)

Instructions by the examiner:

- Examine the eye of this patient. Or, look at the eyes. What are your findings?

Presentation of a Case

- The pupil of right (or left) eye is dilated than other, regular (or circular).
- It does not react to light immediately, but when light is focused for a long time, it constricts slowly.
- Eye movements: Normal, no diplopia.

My diagnosis is **Holmes–Adie pupil**.

Q: What **else** do you want to examine?

A: Tendon jerk (knee and ankle) on the same side: both may be lost. It is then called **Holmes–Adie syndrome**.

Q: What is the **site of lesion**?

A: Ciliary ganglia (due to post ganglionic parasympathetic denervation).

Q: What is the **significance** of Holmes–Adie pupil?

A: It is a benign condition, should not be confused with AR pupil.

Q: What is **Holmes–Adie pupil**?

A: It is an abnormality characterized by absent or delayed pupillary constriction to light or accommodation. If exposed to light for prolonged period, pupil may constrict slowly. If then exposed to dark for long time, the pupil dilates slowly. During accommodation, after some delay, abnormal pupil constricts slowly, may be smaller than normal.

It is also called **myotonic pupil**, which is a benign condition, common in young women, usually unilateral (80%), rarely bilateral. Hence, pupil appears unequal. It may be associated with loss of knee and ankle jerk on the same side. Its cause is not known.



Holmes–Adie pupil (dilated right pupil)

BRIEF DISCUSSION ABOUT DIFFERENT TYPES OF PUPIL

Q: What are the causes of **constricted pupil (miosis)**?

A: As follows:

- Horner's syndrome.
- AR pupil.
- Pontine haemorrhage.
- Senility (pupil in old age tends to be small, may be irregular).
- Morphine.
- Miotic drugs (pilocarpine and physostigmine).
- Poisoning (organophosphorus, opium and trichloroethanol).



Miosis (Right eye)



Mydriasis (Left eye)



Anisocoria

Q: What are the causes of **dilated pupil (mydriasis)**?

A: As follows:

- IIIrd nerve palsy.
- Holmes–Adie pupil.
- Optic nerve lesion (optic neuritis or retrobulbar neuritis).
- Mydriatic drugs (atropine and homatropine).
- Other drugs (tricyclic antidepressant, amphetamine).
- Datura poisoning.
- Fixed dilated pupil (occurs in brain death, also in deep coma).

Q: What are the causes of **unequal pupil (anisocoria)**?

A: As follows:

- Physiological anisocoria in normal eye (20%).
- Iritis.
- Syphilis.
- Holmes–Adie pupil.
- Mydriatic drug in one eye.
- Blindness or amblyopia in one eye (pupil is large in affected eye).
- Cerebrovascular disease (CVD).

Q: What are the causes of **absent light reflex, but present accommodation reflex**?

A: As follows:

- AR pupil.
- Midbrain lesion.
- Ciliary ganglion lesion.

Q: What are the causes of **absent accommodation reflex**, but **normal light reflex**?

A: As follows:

- Cortical lesion (cortical blindness).
- Parkinson's disease due to encephalitis lethargica.

Q: What is **reverse AR pupil**?

A: In reverse AR pupil, the pupils react to light but not to accommodation. It is found in encephalitis lethargica due to epidemic of von Economo's encephalitis that causes parkinsonism.

Q: What is the **afferent and efferent pathway of light reflex**?

A: Afferent is through optic nerve and efferent is through the IIIrd cranial nerve.

Q: What is the **nerve pathway responsible for light reflex**?

A: As follows:

- Afferent pathway: Optic nerve > lateral geniculate body > pretectum of mid brain.
- Efferent pathway: Edinger–Westphal nucleus in mid brain > 3rd nerve > pupil.

Q: What is **Marcus–Gunn phenomenon or pupil**?

A: In this disorder, direct reflex is brisk on exposure to light. However, when light is alternately focused from one eye to other, the pupil on the affected side dilates slowly, when exposed to light. It is found in optic neuritis. The mechanism is as follows:

- When light is focused on healthy eye, a rapid pupillary constriction occurs in both eyes. When light is focused again on the affected eye, the eye fails to transmit the message to continue the constriction as quickly as normal. As a result, pupils have time to recover and dilate, despite the light shining on abnormal eye.
- Direct and consensual reflex are normal when the eyes are tested separately. Fundoscopy should be done to see the evidence of optic neuritis.

N.B. Read the following points in relation to pupil of unconscious patients:

- *One pupil is dilated, fixed to light: Indicates herniation of uncus of temporal lobe (coning) and compression of IIIrd nerve.*
- *Pinpoint fixed pupil: Indicates pontine haemorrhage.*
- *Midpoint and slightly dilated pupil indicates damage to the midbrain with interruption of pupillary light reflex.*
- *Midpoint pupil that reacts to light indicates coma of metabolic origin and central nervous system depressant drugs.*
- *Fixed dilated pupil (bilateral): Indicates brain death and deep coma.*

EXOPHTHALMOS

Instructions by the examiner:

- Look at the face. What are your findings? What else do you want to examine? Examine the eyes.

Proceed as follows:

1. Look at the eyes from front, comment about sclera that is visible between upper eyelid and upper limbus of cornea.
2. Look any swelling of eyelids, congestion of sclera, chemosis (oedema of conjunctiva), corneal ulcer, thyroid stare (a frightened expression).
3. Look at the eyes from behind to confirm proptosis (eyeball may be visible above the supraorbital ridge). Place a paper between the supraorbital ridge and maxillary prominence (note the space between this).
4. If obvious exophthalmos, note the following points:
 - **Lid retraction** (by inspection, ask the patient to look straight): The upper eyelid is retracted and sclera above the upper margin of corneal limbus is visible (normally 1/3rd of cornea is covered by upper eyelid).
 - **Lid lag** (ask the patient to follow your finger down): Upper eyelid fails to follow the finger (called **von Graefe's sign**).
 - Ask the patient to **wrinkle** the forehead (may be absent, called **Joffroy's sign**).
 - See the movement of eyeball both horizontally and vertically (if the movement is absent with exophthalmos, it is called **exophthalmic ophthalmoplegia**).
 - During movement: Ask the patient about **diplopia**.
 - Test for **convergence** (impaired convergence is called **Möbius sign**).
5. Now examine the following points:
 - Signs of thyrotoxicosis (warm sweaty hands, tremor of out-stretched hands and tachycardia).
 - Signs of hypothyroidism (puffy face, baggy eyelids, loss of outer 1/3rd of eyebrows, coarse dry skin, non-pitting oedema, slow relaxation of ankle jerk).
 - Examine the thyroid gland (there may be diffuse enlargement in Graves disease).

Presentation of a Case (Bilateral or Unilateral Exophthalmos):

- There is bilateral (or unilateral) exophthalmos (as evidenced by sclera above the upper limbus is visible, more marked on right or left).
- Eyelids are swollen, there is chemosis, redness and congestion of conjunctival vessels and corneal ulcer.
- Eye movement is impaired of right or left eye (mention in which direction). This indicates ophthalmoplegia.
- There is diplopia on looking (mention in which direction).
- Impaired convergence (Möbius sign).
- Mention about lid lag, lid retraction and wrinkling of forehead (if any).

My diagnosis is **Graves' disease**.

N.B. For details, see in Graves' disease. (chapter Endocrinology).

Q: What is the **difference** between proptosis and exophthalmos?

A: It is synonymous, it means protrusion of eyeball (according to some authority: If unilateral, it is called proptosis and if bilateral it is called exophthalmos). It is assessed by Hertel exophthalmometer (normally <20 mm).



Unilateral exophthalmos (right)



Bilateral exophthalmos



Bilateral exophthalmos
(Graves' disease)

Q: What are the **eponyms of signs** of Graves exophthalmos?

A: As follows

- Lid retraction: **Dalrymple sign**.
- Lid lag: **von Graefe's sign**.
- Failure of wrinkling forehead: **Joffroy's sign**.
- Failure of convergence: **Möbius sign**.
- Incomplete and infrequent blinking: **Stellwag sign**.
- Fixed staring look: **Kocher's sign**.
- Tremor of closed eye lid: **Rosenbach's sign**.
- Weakness of at least one extra ocular muscle: **Ballet's sign**.
- Paralysis of extra ocular muscle: **Jendrassik's sign**.
- Resistance to pulling down the retracted eyelid: **Grove sign**.

Q: What are the **causes** of exophthalmos?

A: As follows:

Cause of unilateral exophthalmos:

1. Graves' disease (common cause).
2. Orbital cellulitis.
3. Retro-orbital deposition found in:
 - Lymphoma.
 - Leukaemia.
 - Secondary deposit.
 - Hydatid cyst.
4. Tumours of the orbit:
 - Neurofibroma.
 - Sphenoidal ridge meningioma.
 - Osteoma.
 - Glioma (from optic nerve sheath).
 - Dermoid.

Cause of bilateral exophthalmos:

1. Graves disease (common cause).
2. Cavernous sinus thrombosis.
3. Carotico-cavernous fistula.
4. Others:
 - Hand–Schuller–Christian disease.
 - Cranio-stenosis.
 - Hypertelorism.
 - Apparently in severe myopia (eye is longer than normal).
 - Bilateral retro-orbital deposition (e.g., lymphoma, leukaemia).

Q: What investigations do you suggest?**A:** As follows:

- Thyroid function tests (for Graves disease, see chapter on Endocrinology).
- Orbital ultrasonogram.
- CT scan of orbit (shows enlargement of extra-ocular muscles, compression in optic nerve and proptosis).

Read the following topics carefully:

- **Cavernous sinus thrombosis:** Usually follows infection of nose, orbit or face. The patient is very toxic, with high temperature. Eyeballs are very painful and congested. Urgent treatment is necessary.
- **Carotico-cavernous fistula:** There is pulsating exophthalmos and conjunctival congestion. A bruit is heard over the orbit, the intensity of which may be reduced by pressing over the carotid artery. Carotico-cavernous fistula is due to rupture of infraclinoid part of internal carotid artery to the cavernous sinus, usually due to trauma or spontaneous. This may require neurosurgical intervention. In 10% cases, there may be small fistula, which resolves spontaneously.

NYSTAGMUS

Instructions by the examiner:

- Examine the eyes. Or, examine the movement of eye. What are your findings?

Proceed as follows:

1. Ask the patient to sit, look straight in front and see whether nystagmus is present or not:
 - If present in central gaze: likely to be ocular nystagmus (fixation nystagmus).
 - If absent, then see in lateral gaze. If present, it is called gaze nystagmus.
2. Now see any nystagmus during movement of eyeball (horizontal or vertical):
 - Keep your finger straight in front of the eye (not below), 2 to 3 feet from the patient.
 - Move the finger laterally, the patient should follow the finger up to 30° to the left and right, keep your finger for 5 seconds (a guide of 30°—limbus and caruncle meet in adducting eye).
 - Do not move beyond 45° from central (beyond that nystagmus may be physiological).
3. Observe, whether it is horizontal or vertical or rotatory.
4. Whether it is jerky or pendular and faster component in which direction.
5. During movement, observe whether nystagmus is present in abducting eye. At the same time, observe any failure of adduction of other eye (called **internuclear** ophthalmoplegia, which is also called **ataxic nystagmus**).

Presentation of a Case (Jerky Nystagmus): Case No. 1:

- There is nystagmus in the right (or left) eye on lateral movement, faster component towards the right (or the left) side.
- No other abnormality in eye movement.
- Diplopia is absent.

My diagnosis is **Horizontal, jerky nystagmus**.

Q: What do you think is the **cause** in this case?

A: May be cerebellar lesion (on affected side) or vestibular lesion (on contralateral side).

Q: What **else** do you want to examine?

A: As follows:

- Cerebellar signs (see in chapter **Neurology**).
- History of vertigo, deafness and tinnitus (suggests vestibular nystagmus).
- History of drugs such as phenytoin and other anti-convulsants, barbiturates, alcohol, benzodiazepines (all these may cause nystagmus).
- Nystagmus may present by movement of head to one side (called positional nystagmus, found in benign positional vertigo).

Q: What is the **cause of vertical nystagmus**?

A: Due to brain stem lesion.

- Nystagmus on downward gaze: Lesion in foramen magnum (involving medulla).
- Nystagmus on upward gaze: Lesion on the floor of fourth ventricle (involving midbrain).

Q: What are the **sites of lesion** that produce nystagmus?

A: As follows:

- Cerebellar lesion.
- Vestibular lesion (central and peripheral).
- Brain stem.

Presentation of a Case (Internuclear Ophthalmoplegia): Case No. 2:

- On lateral movement, there is nystagmus in the abducting eye and failure of adduction of other eye (dissociation of movement of other eye).
- On covering the abducting eye, adduction of other eye is normal.
- No other abnormality.

My diagnosis is **Internuclear ophthalmoplegia** (also called ataxic or dissociated nystagmus).

Q: What is the **site of lesion**?

A: Medial longitudinal fasciculus (MLF) in the brain stem. MLF connects VIth nerve nucleus on one side to IIIrd nerve nucleus of the opposite side of brain stem.

Q: What are the **causes of internuclear ophthalmoplegia**?

A: As follows:

- Multiple sclerosis (common cause).
- Pontine glioma.
- Vascular cause (CVD).
- Wernicke's encephalopathy (also there is ocular palsy, loss of pupillary reflex, ataxia and Korsakoff's psychosis).
- Encephalitis.
- Phenytoin toxicity.

READ THE FOLLOWING TOPICS IN RELATION TO NYSTAGMUS

Q: What is **nystagmus**?

A: It is the involuntary, rhythmical and oscillatory movement of the eyes due to inability to maintain the posture of eyes, owing to lack of balance of opposing ocular muscles. It is defined by the direction of fast phase and is exaggerated on gaze to that side. Nystagmus must be sustained for more than a few beats to be significant. It may be jerky or phasic, pendular or ataxic (internuclear ophthalmoplegia).

Q: What are the **types of nystagmus**?

A: As follows:

1. According to the direction:
 - Horizontal.
 - Vertical.
 - Rotatory.
2. According to the site of lesion:
 - Cerebellar nystagmus (towards the site of lesion).
 - Vestibular nystagmus (away from the site of lesion).
 - Brain stem lesion (usually vertical nystagmus, may be in other direction).

3. Others:

- Positional nystagmus (associated with benign positional vertigo).
- Ocular or fixation nystagmus (usually pendular type).
- Optokinetic.
- See-saw nystagmus.

Q: What is jerky nystagmus?

A: Jerky or phasic nystagmus is characterized by eye movement faster in one direction than other. Usually seen in horizontal direction, elicited on lateral gaze in one or both directions. Causes are cerebellar lesion, vestibular lesion or lesions of their connection in the brain stem.

Q: What is pendular nystagmus?

A: In this type, oscillations are equal in speed and amplitude in both directions of eye movement, usually seen in central gaze. Cause is poor visual acuity (in severe refractive error or macular disease), usually congenital and asymptomatic.

Q: What is ataxic nystagmus?

A: In this type, on looking to one side, nystagmus is present in the abducting eye and there is failure of adduction of other eye. It is also called dissociated nystagmus and is present in internuclear ophthalmoplegia.

Q: What are the causes of horizontal nystagmus?

A: As follows:

1. Cerebellar.
2. Vestibular nystagmus.
3. Brain stem lesion.
4. Others:
 - Ocular or fixation nystagmus (usually pendular type).
 - Optokinetic.
 - In normal person, in extreme lateral gaze.

Q: What are the causes of vertical nystagmus?

A: As follows:

- Brain stem lesion: up beating (midbrain lesion) and down beating (medulla with foramen magnum lesion).
- Rarely, ocular nystagmus.

Q: What are the causes of vestibular nystagmus?

A: Vestibular nystagmus is usually horizontal or rotatory, not vertical. It is 2 types: peripheral and central.

1. Peripheral: Lesion in labyrinth or vestibular nerve. Fast component of nystagmus is opposite to the site of lesion, may be associated with cochlear lesion. Causes are:
 - Labyrinthitis (may be viral).
 - Meniere's disease.
 - Acoustic neuroma.
 - Head injury.
 - Middle ear disease.
 - Vestibular neuronitis (presents with acute vertigo, tinnitus and deafness).

2. Central: Lesion is in vestibular nuclei. Causes are:

- CVD.
- Multiple sclerosis.
- Neoplasm.
- Alcohol.
- Anti-convulsant drugs.

Q: What is optokinetic nystagmus?

A: It occurs when the patient follows a rapidly moving scene (e.g., during travelling in a train, eye remains fixed to a telegraph pole). It is a normal phenomenon.

Q: What is see saw nystagmus?

A: In this condition, one eye raises and turns in, the other eye falls and turns out. It is due to parasellar tumour.

Q: What is positional nystagmus?

A: In this condition, nystagmus is present in certain position and rapid movement of the head.

- It can be detected by **Hallpike's test**, in which the patient should lie on the back, support the head and allow to fall below horizontal plane and turn to one side.
- After a few seconds, rotatory nystagmus and vertigo develop. If the position is maintained, fatigue occurs after 10 to 20 seconds, nystagmus and vertigo disappear.
- If the test is repeated immediately, there is little response (adaptation). It is usually associated with benign positional vertigo.

Causes: Calcific degeneration of utricle and saccule of inner ear causes small particles to fall on the cupola of semicircular canal during the movement of head.

SUBHYALOID HAEMORRHAGE

Instructions by the examiner:

- Perform fundoscopy.

Presentation of a Case

- There is haemorrhage with crescentic shape or upward concavity or, horizontal upper margin in the right eye.
- Other part of the retina is normal (there may be bleeding spots in the retina).

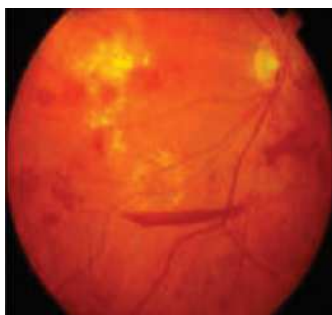
My diagnosis is **Subhyaloid haemorrhage**.

Q: What are the **typical findings** in subhyaloid haemorrhage?

A: Sharply demarcated pre-retinal haemorrhage with crescentic or upward concavity (called subhyaloid haemorrhage). If the patient is in supine position, then the fluid level is not seen. Retinal haemorrhage and mild papilloedema may be seen. Haemorrhage may extend into the vitreous humour, which is called Terson syndrome.

Q: What is the **presentation** of subhyaloid haemorrhage?

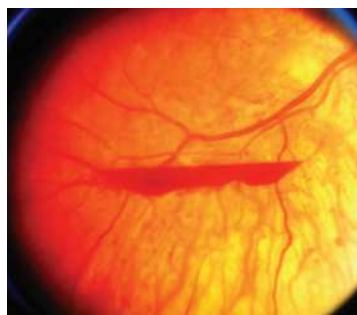
A: The patient presents with sudden painless loss of vision. There may be blurring or floaters or black spots with or without flashing lights. Features of subarachnoid haemorrhage are present.



Subhyaloid haemorrhage with exudates and haemorrhage



Subhyaloid haemorrhage (large)



Subhyaloid haemorrhage (typical)

Q: What are the **causes** of **vitreous haemorrhage**?

A: As follows:

- Subarachnoid haemorrhage.
- Diabetes mellitus.
- Hypertension.
- Blood dyscrasia.
- Trauma.

Q: What is the **cause** of **subhyaloid haemorrhage**?

A: Subarachnoid haemorrhage (subhyaloid haemorrhage is pathognomonic of SAH).

Q: What are the features of SAH?**A:** As follows:

- Sudden severe headache, usually occipital (thunder clap headache or struck by a hammer).
- Nausea, vomiting.
- Loss of consciousness.
- Neck rigidity.
- Kernig's sign may be positive.
- Fundoscopy shows subhyaloid haemorrhage (upward concavity, boot shaped).

Q: What are the causes of SAH?**A:** As follows:

- Rupture of berry aneurysm (commonest cause, 80%).
- Arteriovenous malformation (AVM).
- Head injury.

Q: What investigations do you suggest for SAH?**A:** As follows:

- CT scan of head (preferable than MRI).
- CT angiogram may be done if needed.
- Lumbar puncture and CSF study may be done.
- Cerebral angiography may be needed later to find out the source.

Q: What are the findings in CSF?**A:** As follows:

- High pressure.
- Frankly haemorrhagic fluid.
- Xanthochromia (when kept for some hours).

Q: What are the causes of frank blood in CSF?**A:** Trauma, SAH.**Q: How will you differentiate CSF finding of SAH from trauma?****A:** As follows:

- In trauma: initial sample is mixed with blood, but subsequent samples show clear fluid or less blood.
- In SAH: All the test tubes have fluid mixed with blood. Xanthochromia is present if the fluid kept for hours (absent in traumatic blood).

Q: How to treat?**A:** As follows:

- Control of hypertension.
- Oral nimodipine.
- Neurosurgical intervention.

N.B. Remember the following points regarding SAH:

- *More common in women.*
- *Immediate mortality is 30%.*
- *Chance of recurrence is 40% in 4 weeks and 3% annually.*
- *Berry aneurysm arises from bifurcation of circle of Willis.*
- *If the patient with SAH deteriorates, it indicates either rebleeding or cerebral infarct due to reflex vasospasm of the cerebral vessels (which can be prevented by using nimodipine).*

CHOROIDO-RETINITIS

Instructions by the examiner:

- Perform fundoscopy.

Presentation of a Case:

- There are multiple pigmented patches with whitish or greyish areas within these, seen on the upper and temporal side of the right eye.
- There is no haemorrhage, but exudates are present. Retinal vessels are normal.

My diagnosis is **Choroido-retinitis**.

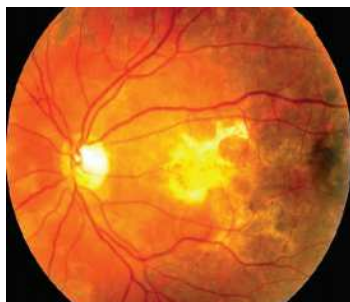
Q: What are the **causes** of choroido-retinitis?

A: As follows:

- Toxoplasmosis.
- Tuberculosis.
- Sarcoidosis.
- Syphilis.
- Toxocariasis.
- Behcet's disease.
- Cytomegalo virus infection.
- HIV (AIDS).



Choroido-retinitis in toxoplasmosis



Choroido-retinitis in TB



Choroido-retinitis in sarcoidosis

Q: Why there is **pigmentation**?

A: Due to exposed sclera in old choroiditis, causing atrophy of choroido-retina. Also proliferation of retinal pigment epithelium.

Q: What are the **presentations** with choroido-retinitis?

A: Patient may complain of reduced vision, floaters and redness of eye. Features of primary disease may be present.

Q: What are the **typical findings** of **CMV retinitis**?

A: There may be haemorrhage, oedema and exudate. Typically, it looks like cottage cheese and ketchup appearance.

Q: How would you **treat CMV** retinitis?

A: Ganciclovir or foscarnet (intravenous).

Q: What are the **other causes** of pigmentation in retina?

A: As follows:

- Photocoagulation.
- Retinitis pigmentosa.
- Malignant melanoma.
- Racial (tigroid fundus).

Q: What is the **prognosis**?

A: Poor, if fovea is involved. Also depends on aetiology.

Q: What are the retinal changes in **AIDS**?

A: As follows:

- Due to CMV (see above).
- Due to HIV—cotton wool spots.

RETINAL DETACHMENT

Instructions by the examiner:

- Perform fundoscopy.

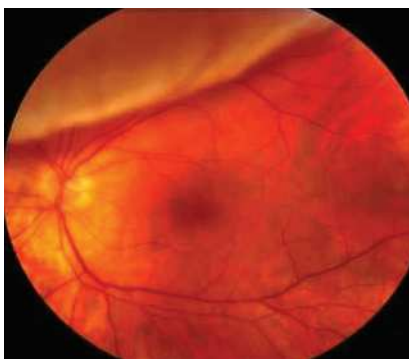
Presentation of a Case:

- The retina is opaque and grey in the left eye (no pink colour).
- There is ballooning detachment with numerous folds (indicates large collection of subretinal fluid).

My diagnosis is **Retinal detachment**.



Retinal detachment



Retinal detachment

Q: What are the causes?

A: As follows:

- Uncontrolled diabetes mellitus.
- Retinal surgery (loss of vitreous following cataract surgery).
- Trauma (perforating eye injury).
- Chronic inflammation.
- Posterior vitreous detachment.
- Severe myopia.
- Systemic disease: Hypertension, toxæmia of pregnancy, chronic glomerulonephritis, retinal venous occlusive disease, retinal vasculitis.

Q: What are the presentations of retinal detachment?

A: As follows:

- Flashes of bright light (photopsia) in the peripheral part of vision.
- Floaters in the eye.
- Feeling of heaviness in the eye.
- Blurring of vision.
- Blindness or shadow starting peripherally and progressing centrally. The patient typically describes a curtain or veil being drawn over the visual field.
- Loss of central vision.

Q: What is the mechanism of retinal detachment?

A: Separation within the retina between the photoreceptors and retinal pigmented epithelium, characterized by collection of fluid and blood in this space.

DRUSEN

Instructions by the examiner:

- Perform the fundoscopy.

Presentation of a Case:

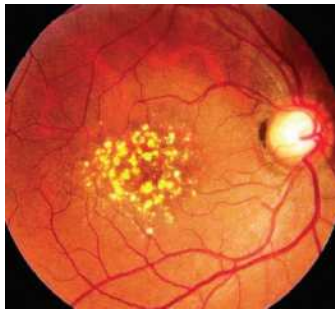
- There are multiple discrete, round, pale yellow dots of variable size and shape scattered around the macula and posterior pole of the eye.
- Visual acuity is normal. No visual field defect.

My diagnosis is **Retinal drusen (which is associated with age related or senile macular degeneration)**.

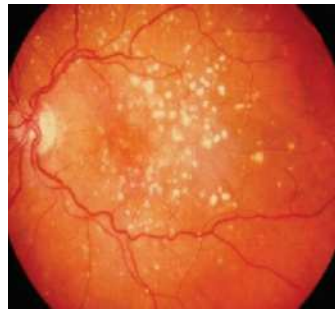
Q: What is Retinal Drusen?

A: These are the yellow or yellowish white or yellow grey spots, usually scattered throughout the macula and posterior pole of the eye. These are due to accumulation of extracellular material between the retinal pigment epithelium and Bruch's membrane, usually found after 50 years of age.

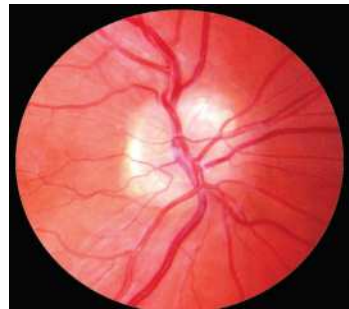
When the number of drusen present >5 and large drusen $>63\ \mu\text{m}$ in diameter, it indicates age related macular degeneration which may be associated with pigmented change in retina. In such case, there is reduced visual acuity and visual field defect. Drusen may be normally found with increasing age. Patient above 50 years may have one small drusen ($<63\ \mu\text{m}$) in one or both eyes.



Macular drusen



Drusen involving macula and retina



Optic nerve drusen

Q: What are the constituents in Drusen?

A: Drusen is composed of vitronectin, lipids, amyloid associated proteins, complements factors and trace elements (Zinc).

Q: What are the complications of age related macular degeneration?

A: One of the important cause of blindness above 60 years of age.

Q: How common is age related macular degeneration (ARMD)?

A: It is the common cause of blindness over 60 years of age.

Q: What are the risk factors?

A: Age above 60 years, smoking, hypertension, exposure to sunlight, cataract surgery, positive family history.

Q: What are the **types**?

A: Dry and wet ARMD. Dry is the common form.

Q: How to **treat**?

A: No specific therapy, mostly supportive:

- Regular follow up with ophthalmologist.
- In dry ARMD: Vitamin C, E, Lutein, zeaxanthin, zinc, copper may be given, which delay the progression to wet ARMD.
- Wet ARMD: Anti VEGF drugs and LASER surgery may be helpful.

RETINAL ARTERY OCCLUSION

Instructions by the examiner:

- Perform fundoscopy of this patient.

Presentation of a Case No. 1 (Mention Right or Left):

- The retina is pale, arterioles are thin and scanty.
- There is cherry red spot at the macula (underlying choroidal circulation is intact). Patient's affected eye is blind.

My diagnosis is **Central retinal artery occlusion (CRAO)**.

Q: What else do you like to examine in this patient?

A: As follows:

- Carotid bruit.
- In heart: valvular lesion, atrial fibrillation, evidence of infective endocarditis, ASD (causes paradoxical embolism).
- Evidence of giant cell arteritis (history of headache, temporal artery tenderness or thickening).
- BP (high).
- History of diabetes mellitus.

Presentation of a case no. 2 (Mention Right or Left):

- The retina is pale in the upper and outer quadrant, arterioles are thin and scanty at the same area.

My diagnosis is **Branched retinal artery occlusion** involving superior temporal artery (may be associated with visual field defect of the corresponding area).

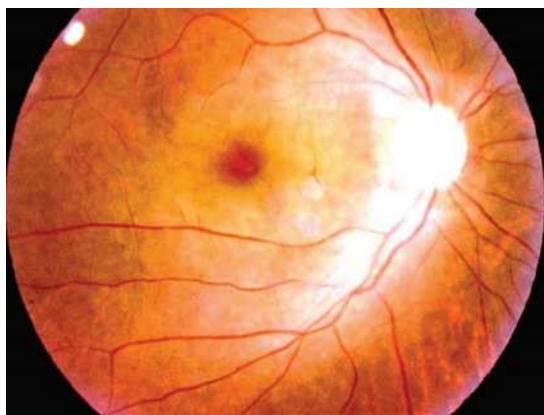
Q: What are the causes of retinal artery occlusion?

A: As follows:

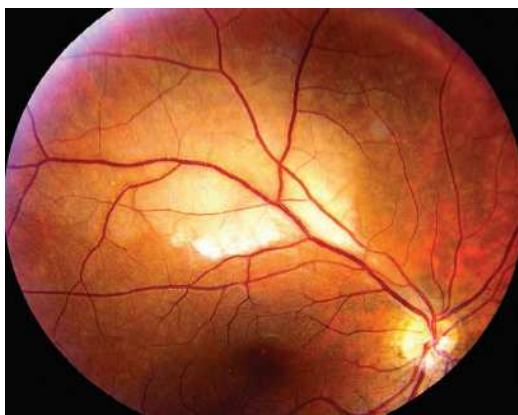
- Hypertension.
- Diabetes mellitus.
- Atherosclerosis.
- Cardiac cause: atrial fibrillation, myxoma, infective endocarditis.
- Giant cell arteritis.

Q: What are the presentations or symptoms of the patient?

A: Sudden painless loss of vision. In branched retinal artery occlusion, there may not be any symptom.



Central retinal artery occlusion



Branched retinal artery occlusion

Q: How to treat CRAO?**A:** As follows:

- Ocular massage (it helps to dislodge the embolus).
- Oral or IV acetazolamide (it lowers intra-ocular pressure).
- Carbogen therapy (mixed inhalation of 95% O₂ and 5% CO₂).
- Paracentesis from anterior chamber of eye.

N.B.: CRAO may be associated with Marcus Gunn pupil, secondary optic atrophy, cherry red spot.

MISCELLANEOUS OCULAR ABNORMALITY

Ocular Prosthesis (Artificial Eye): One eye looks glazy, other eye is normal. On the affected eye, patient is blind and light reflex is absent.

Indication of enucleation:

- Traumatic damage.
- Suspicion of malignancy (such as retinoblastoma, melanoma).
- End stage glaucoma.
- Endophthalmitis.
- Congenital cystic eye.



Ocular prosthesis



Corneal arcus



Pingueculae

Corneal Arcus: It is a crescentic whitish opacity, like a line near the periphery of cornea. Usually, starts at lower part, ultimately completes the circle.

- Corneal arcus indicates annular infiltration of lipid in the peripheral rim of cornea.
- A normal finding in the elderly (called arcus senilis).
- Sometimes, it is associated with hypercholesterolaemia, specially in young patients (called arcus juvenilis). May also be present in type IV hyperlipoproteinaemia.
- Usually no treatment in elderly. Lipid lowering drugs in hypercholesterolaemia and hyperlipoproteinaemia, specially in younger patient.

Pingueculae: Yellowish thickening of conjunctiva, may be on either side of cornea, progresses towards cornea, but does not cover it. It is due to the hyaline degeneration of elastic tissue. Causes are:

- In the elderly, exposure to dust and fume.
- Gaucher's disease.

Band Keratopathy: It is the subepithelial deposition of calcium salt in the cornea with a clear zone separated from limbus. Causes are:

- Hypercalcaemia due to any cause.
- Iridocyclitis in children.
- Idiopathic in children.
- Phthisis bulbi.

Treatment: Chelating agents, such as sodium versenate is helpful.



Kayser–Fleischer ring



Blue sclera



Band keratopathy

Kayser–Fleischer Ring (KF ring): It is a greenish-brown discolouration at the corneal margin, usually appears first at the upper periphery, then encircles the whole cornea. It is due to deposition of copper in Descemet's membrane of cornea. May not be seen by naked eye, requires slit lamp examination. Presence of KF ring is pathognomonic of Wilson's disease. Present in neurological Wilson's disease. It may be absent or less in young children and rarely found in primary biliary cirrhosis. KF ring disappears with treatment.

Blue Sclera: Causes are:

- Isolated.
- Osteogenesis imperfecta.
- Marfan's syndrome.
- Homocystinuria.
- Ehlers–Danlos syndrome.
- Pseudoxanthoma elasticum.

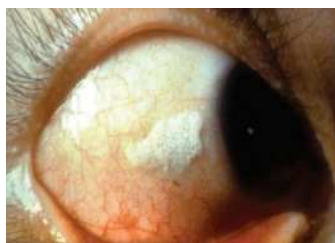
Bitot's Spot: These are white plaques of desquamated, thick conjunctival epithelium, triangular in shape, usually found in young patients due to vitamin A deficiency. Sometimes, may occur on exposure to dust and glare.

Q: What are the eye problems that occur in vitamin A deficiency?

A: As follows:

1. Night blindness.
2. Xerophthalmia:
 - Initially, xerosis conjunctivae (dry, thick, pigmented bulbar conjunctiva associated with smoky appearance), then Bitot's spot.
 - Later, when dryness spreads over the cornea, it is dull, hazy and lacks lustre due to keratinization called xerophthalmia.
3. Keratomalacia: Corneal opacity, ulcer and dissolution leading to blindness.

Treated with vitamin A, otherwise blindness may occur.



Bitot's spot



Bitot's spot



Keratomalacia

Q: What are the causes of sudden blindness?

A: Sudden blindness may be in one eye or both eyes:

Causes of mono ocular (one eye) blindness:

- Trauma to the eye.
- Central retinal artery occlusion.
- Central retinal vein occlusion.
- Giant cell arteritis.
- Optic neuritis or retrobulbar neuritis.
- Acute ischaemic optic neuropathy.
- Migraine.
- Others: acute glaucoma, retinal detachment, Leber's optic atrophy, functional.

Causes of binocular (both eyes) blindness:

- Bilateral occipital lobe infarction.
- Bilateral occipital lobe trauma.
- Bilateral occipital nerve damage.
- Methyl alcohol poisoning, may be in quinine and ethambutol toxicity.
- Functional (hysteria).

Q: What are the causes of gradual blindness?

A: Causes of bilateral blindness of gradual onset are:

- Cataract.
- Macular degeneration.
- Diabetic retinopathy (vitreous haemorrhage).
- Optic atrophy.
- Bilateral optic nerve or chiasmal compression.
- Bilateral optic nerve damage (such as tobacco amblyopia).

Q: What is Amaurosis?

A: It means blindness due to any cause.

Q: What is Amaurosis fugax?

A: It is the transient painless loss of vision in one eye due to occlusion of retinal artery or its branches. Usually recovers within 3 to 4 hours.

BRIEF NOTE ON METHANOL POISONING

Q: What is Amblyopia?

A: It means impaired vision not due to refractive error or ocular disease.

Methanol Poisoning: Methanol is a component of varnishes, paint remover, wind shield washer solutions and copy machine fluid. Methanol is metabolized in liver (90%) by alcohol dehydrogenase to formaldehyde and formic acid. Only 10% is excreted unchanged by lungs and kidneys. Clinical features are:

- Early manifestations (by methanol): Nausea, vomiting, abdominal pain, headache, vertigo, dizziness, convulsion, confusion, stupor and coma.
- Later on (by metabolite formic acid): There is retinal injury leading to blindness. Ocular toxicity occurs 15 to 19 hours after ingestion. Metabolic acidosis is also common.
- In severe cases: Bradycardia, myocardial depression and shock.

Treatment:

- Gastric lavage.
- Supportive measures: IV fluid, oxygen.
- Correction of acidosis: Sodium bicarbonate in large dose (alkalinization enhances formic acid excretion).
- In early stage: Ethanol is given (it inhibits methanol oxidation by competing the inhibition of enzyme). 10% ethanol 10 mL/kg IV or 1 mL/kg of 95% ethanol orally.
- Thiamine (100 mg QID), pyridoxine (50 mg QID) and folate (50 mg QID).
- Folinic acid 30 mg IV every 6 hourly. It reduces ocular toxicity (accelerates metabolism of formic acid).
- Dialysis: Indicated, if ingestion of methanol is >30 gm or metabolic acidosis or blood methanol >500 mg/L.

Q: What is Bitemporal Hemianopia?

A: It means the loss of vision on the temporal side in both eyes. Central vision is intact.

Q: What is the site of lesion?

A: Centre of optic chiasma, damaging the fibres from nasal half of retina, as they decussate at chiasma. This will cause loss of both temporal half of visual field.

Q: What are the causes?

A: As follows:

- Pituitary tumour.
- Craniopharyngioma.
- Sarcoidosis.
- Suprasellar meningioma.

Q: What are the presentations?

A: May not be any complaint, but sometimes diplopia. Patient may complain of repeated collision on the sides with another person or door etc.

Q: What investigations do you suggest?

A: As follows:

- Perimetry.
- X-ray skull.
- MRI of brain.
- Pituitary hormone assay.

DERMATOLOGY

11

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DERMATOLOGY

11

'This is a very testing part. It is more difficult than a written test'
—Talley & O'Connor

INTRODUCTION

In any clinical examination of medicine, a few common cases related to dermatology are frequently selected. Most of the diagnosis is obvious on visual impression. The concept of **inspection** is always a valuable starting point during examination of a patient of dermatological diseases.

With the patient's permission, undress the patient and remove the make-up, if possible. A magnifying lens is helpful. Good light, preferably natural, is more appropriate. Feeling the skin by gentle palpation may provide a diagnostic clue.

Examine the patient very carefully and gently. Before presenting the case, describe the lesion precisely as follows:

- Distribution of lesion.
- Colour.
- Size and Shape.
- Any oozing.
- Pattern of lesion (ulcerative, linear, ring like, reticulated, annular).

After inspection, palpate to see tenderness, consistency, temperature and mobility.

Usual instructions by the examiner:

- 'Perform the general examination of this patient' or 'Look at here' (examiner may indicate a part).
What is your diagnosis?
- What else do you want to examine?
- Examine the mouth of this patient. (Any oral ulcer, lichen planus, pigmentation etc.).

In this chapter, a few common dermatological diseases are described with related questions and answers. Only brief discussions are given. Candidates are advised to go through a lot of dermatological cases to develop their skill for spot diagnosis.

Skin consists of 3 layers:

1. Epidermis: It has 5 layers. From top to bottom, the layers are:
 - Stratum corneum (horny layer).
 - Stratum lucidum.

- Stratum granulosum (granular layer).
 - Stratum spinosum (prickle cell or Malpighian layer).
 - Stratum basale (basal layer).
2. Dermis.
 3. Hypodermis or subcutis.

Epidermis is an avascular stratified squamous epithelium, attached to the dermis by basement membrane. Basal cells move outwards towards superficial horny layer and the time taken is four weeks. 95% cells of epidermis are keratinocytes, the remaining 5% are Langerhans cells and melanocytes. There are a few Merkel cells. Dermis contains blood and lymphatic vessels, nerves, muscle, appendages (sweat glands, apocrine glands, sebaceous glands, hair follicles) and immune cells such as mast cells and lymphocytes. It also contains collagen, elastin and ground substances.

Functions of the skin:

1. Protection against chemicals, ultraviolet radiation (UVR), antigens and microbes.
2. Physical barrier against friction and shearing forces.
3. Preservation of a balanced internal environment by preventing loss of water, electrolytes and macro-molecules.
4. Sensation such as pain, touch and temperature.
5. Synthesis of vitamin D and testosterone.
6. Temperature regulation.
7. Maintains body odour and psychosocial factors.

PSORIASIS

Instructions by the examiner:

- Look at here. What is your diagnosis? What else do you like to see?

Presentation of a Case:

- There are multiple, well circumscribed, erythematous plaques with silvery white scales at the knee, scalp and natal cleft (mention the site).

My diagnosis is **Psoriasis**.

Q: What else do you want to examine?

A: I want to see:

- Nails: Pitting, oil spot, cracking of free edges, thickening and subungual hyperkeratosis, onycholysis (it means separation of nail plate from its bed).
- Joints: Psoriatic arthropathy.
- Eye: Iritis (may be blepharitis, keratitis and conjunctivitis).
- Tongue: Geographical tongue.

Q: What are the sites of psoriatic skin lesion?

A: Extensor surfaces of knee, elbow, wrist, back of ear, scalp, hairline, extensor of limbs, sacrum, around the umbilicus, intergluteal cleft and flexures (natal cleft, axillary fold), submammary fold and nails.



Plaque psoriasis



Plaque psoriasis



Guttate psoriasis (front)



Guttate psoriasis (back)

Q: What are the differential diagnoses of psoriasis?

A: Psoriasis may be confused with the following diseases:

- Dermatomyositis (In this case, there will be heliotrope sign, atrophy and poikiloderma).
- Lichen planus (it is usually on flexor surface, associate with Wickham striae, violaceous flat-topped papules and adherent scale).
- Seborrhoeic dermatitis (there is greasy, yellowish scale on eye brows, nasolabial crease, gluteal crease, ears, sternal region, axilla, submammary folds, umbilicus and groin).
- Pityriasis rosea (in which, there is short duration, herald patch and collarette scaling on trunk, upper arms and thighs).
- Subacute lupus erythematosus.
- Secondary syphilis.
- Dermatophytosis (such as tinea corporis, cruris and pedis).

Q: What is **Auspitz sign** and **Koebner's phenomenon** in psoriasis? (or what are the signs to be seen in psoriasis?)

A: As follows:

- Auspitz sign: On removing the scales forcibly, capillary bleeding points may be seen.
- Koebner's phenomenon: Psoriatic lesion is produced when the normal skin of a psoriatic patient is scratched or injured (may occur in surgical scar).

Q: What is **Koebner's phenomenon**? What are the **causes** of Koebner's phenomenon?

A: Koebner's phenomenon is the appearance of isomorphic skin lesions at the site of trauma, burn or scratch mark. Causes are:

- Psoriasis.
- Lichen planus.
- Viral warts (verruca plana).
- Others: vitiligo, pityriasis rubra pilaris, molluscum contagiosum, nummular eczema, Darier's disease.



Koebner's phenomenon



Auspitz sign



Psoriasis in surgical scar

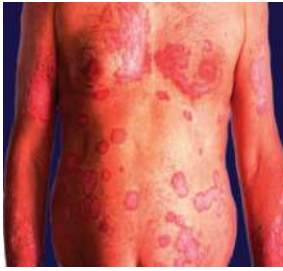


Scalp psoriasis

Q: What are the **factors** that aggravate psoriasis?

A: Aggravating factors are:

1. Trauma.
2. Infections: Streptococcus β -haemolyticus (aggravates guttate psoriasis) and HIV infection.
3. Psychological factors: emotion and anxiety.
4. Drugs:
 - β -Blocker.
 - Antimalarial (chloroquine or hydroxychloroquine).
 - Lithium.
 - Systemic steroid: aggravates after withdrawal of steroid (rebound phenomenon) and also after stopping of prolonged use of local steroid.
 - Angiotensin converting enzyme (ACE) inhibitor.
 - Alcohol.
5. Rarely, sunlight (UVR may worsen).
6. Metabolic (hypocalcaemia, dialysis).



Typical psoriatic patch
with silvery scale



Pustular psoriasis
(palm)



Pustular psoriasis
(back)



Nail pitting

READ THE FOLLOWING TOPICS IN RELATION TO PSORIASIS

Q: What is **psoriasis**? What are the various **types** of psoriasis?

A: It is a chronic inflammatory disease of skin characterized by well defined erythematous plaque with silvery white scales, involving commonly the extensor surface, elbows, knees and sacral regions associated with recurrence and remission. It affects 1 to 2% of the population. 4 types:

- Chronic plaque psoriasis (it is common. Characterized by well demarcated, red with dry silvery white scale. It commonly involves elbow, knee and lower back, but may also involve scalp, nails, flexures, palms).
- Guttate psoriasis (rain drop like psoriasis is a variant, common in children and young adults. An explosive eruption of very small circular or oval plaques appears over the trunk about 2 weeks after a streptococcal sore throat. Majority of the patients develop plaque psoriasis in later life).
- Pustular psoriasis (It may be localized involving palm and sole or rarely generalized, which may be serious).
- Erythrodermic psoriasis (>90% of body surface area become red and scaly).

Q: What is the **pathology** of psoriasis?

A: There is rapid proliferation and abnormal differentiation of epidermis due to hyperproliferation of keratinocyte and infiltration of inflammatory cells (polymorph, T-lymphocyte and other inflammatory cells).

Q: What **investigations** should be done in psoriasis?

A: As follows:

1. Routine:
 - CBC.
 - Liver function test (SGPT, SGOT, Alkaline phosphatase).
 - Serum creatinine.
 - Lipid profile.
 - X-ray chest.
 - Urine R/M/E (to see proteinuria).
 - Serum electrolytes (to see hypokalaemia, hyponatraemia).
 - Serum uric acid (may be high).
 - Serum IgE (to differentiate from atopic dermatitis).

2. To establish the diagnosis, the following procedures may be performed:
 - Skin biopsy for histopathology (definitive).
 - ASO titre (high in guttate psoriasis).
 - Throat swab for C/S (for guttate psoriasis).
 - X-ray of the affected joints (in psoriatic arthritis).
3. To exclude other causes, the following tests may be performed:
 - To exclude syphilis: VDRL, TPHA.
 - To exclude other collagen disease: ANA, anti-ds DNA, anti SS-A, anti SS-B.
 - Skin scraping for fungus.

Q: What are the **histological findings** in psoriasis?

A: As follows:

- Hyperkeratosis, parakeratosis, orthokeratosis.
- Granular layer is absent or thin over the dermal papilla.
- Neutrophilic micro-abscess of Munro in the stratum corneum.
- Spongiform pustule of Kogoj in stratum spinosum.
- Regular elongation of rete ridges, which are club shaped.
- Dermal capillary dilatation and tortuosity surrounded by neutrophil, lymphocyte and histiocytic perivascular infiltrate.



Psoriasis (sub-mammary fold)



Exfoliative dermatitis (body)



Exfoliative dermatitis (body)

Q: What are the **complications** of psoriasis?

A: As follows:

- Psoriatic arthropathy.
- Exfoliative dermatitis.
- Secondary infection.
- Hyperuricaemia and gout.
- Others: amyloidosis, renal failure, hepatic failure and CCF.

Q: How to **treat** psoriasis?

A: As follows:

1. General measures:
 - Explanation and reassurance.
 - Avoid trauma, precipitating drugs and anxiety.

2. Specific treatment:

- Local therapy.
- Systemic therapy.
- Combination therapy.

Local therapy (topical therapy on the lesion):

- Emollient: petrolatum, paraffin, urea (up to 10%), olive oil.
- Salicylic acid (0.5%): It is keratolytic, used to soften and remove the scale from psoriatic plaques.
- Crude tar (3 to 5%): It inhibits DNA synthesis.
- Dithranol: It inhibits DNA synthesis.
- Calcipotriol: It is a vitamin D3 analogue. It inhibits epidermal proliferation and restores normal horny layer, very effective in the treatment of plaque and scalp psoriasis. It may cause hypercalcaemia and hypercalciuria.
- Tazarotene: Third-generation topical retinoid. It acts by modulating keratinocyte differentiation and hyperproliferation, also by suppressing inflammation.
- Topical steroid.
- UVR therapy: Narrow band UVB (peak emission around 311 nm), more effective than broad-band UVB. It may cause burning.
- Tacrolimus and pimecrolimus: Helpful for thin lesions in areas prone to atrophy or steroid acne.
- Excimer laser: Indicated in patient with stable recalcitrant plaques particularly in the elbow and knee region.

Systemic therapy:

- PUVA (psoralen and UVA): Long term use may cause squamous cell carcinoma, basal cell carcinoma and melanoma.
- Retinoid (acitretin): Helpful for arthritis and psoriasis (especially pustular and also plaque). Avoid in young female (as it is teratogenic).
- Methotrexate, azathioprine or cyclosporine may also be used.
- Biologic agents: Anti-TNF- α such as infliximab, etanercept, adalimumab and efalizumab.
- Other drugs: Tacrolimus, mycophenolate mofetil, hydroxyurea and thioguanine.

Combination therapy:

- MTX plus topical agent.
- MTX plus retinoid.
- Retinoid plus PUVA.
- MTX plus infliximab.

For nail disease:

- Systemic agents.
- Topical retinoids.
- Local triamcinolone injection.
- Topical fluorouracil.

Q: Name the **drugs** that will be helpful both in psoriasis and arthritis.

A: Methotrexate, azathioprine and acitretin.

ERYTHEMA MULTIFORME AND STEVENS–JOHNSON SYNDROME

Instructions by the examiner:

- Look at here. What is your diagnosis? Or, perform general examination of this patient.

Presentation of a Case: No. 1:

- There are multiple erythematous, maculopapular, urticarial, vesicular and bullous lesions involving the skin of palm, leg and foot (mention the site), with few target lesions.

My diagnosis is **Erythema multiforme**.

Q: What else do you want to examine? Why?

A: Oral cavity for mouth ulcer. If mouth ulcer is present with skin lesion, the diagnosis is **Stevens–Johnson syndrome**.

Q: What is the **important** skin lesion in erythema multiforme?

A: Target lesion (also called **iris lesion** or **Bull's eye lesion**). In this lesion, there is central pallor or dusky purpura with oedema and peripheral redness.



Erythema multiforme
(target lesion on hands)



Erythema multiforme
(target lesion on thigh)



Stevens–Johnson
syndrome (face)



Stevens–Johnson
syndrome (body)

Q: What are the **differential diagnoses**?

A: As follows:

- Drug reaction.
- SLE.
- Pemphigus vulgaris or bullous pemphigoid.
- Dermatitis herpetiformis.
- Urticaria or urticarial vasculitis.

Presentation of a Case: No. 2:

- Multiple erythematous, maculopapular, urticarial, vesicular and bullous lesions involving the skin of whole body.
- Some vesicles are ruptured with multiple ulcers and crust formation with oozing and red margin.
- Few mouth ulcers with red margin are present at buccal mucosa.

My diagnosis is **Stevens–Johnson syndrome (SJS)**.



Toxic epidermal necrolysis



Staphylococcal scalded skin syndrome



SJS-TEN overlap (face and body)

Q: What is erythema multiforme? What is SJS?

A: As follows:

- Erythema multiforme is an acute inflammatory reaction in the skin and mucous membrane, characterized by multiple erythematous skin lesions, such as macules, papules, vesicles, bullae and target lesions involving the extensor surfaces of limbs. It is due to circulating immune-complex that follows 7 to 14 days after precipitating factors (such as infections and drugs). It is usually self limiting, resolves in 3 to 6 weeks, may recur.
- SJS is the severe form of erythema multiforme with widespread vesico-bullous lesion in the skin and mucous membrane of mouth, eyes and genitalia associated with severe constitutional symptoms.

N.B. Remember the following points:

- In SJS, <10% body surface area (BSA) involvement.
- 10 to 30% BSA involvement is called SJS-TEN (toxic epidermal necrolysis) overlap cases.
- When >30% of BSA involvement, it is called TEN. Patient who initially present with SJS may progress to TEN.

Q: What are the causes of erythema multiforme?

A: As follows:

- Infections: HSV type 1 and *Mycoplasma pneumoniae* (common). Other infections: *Streptococcus* and *Histoplasma*.
- Drugs: Sulfonamides, carbamazepine, barbiturate, thiacetazone, penicillin, phenytoin.
- Idiopathic (50% cases).
- Others: Malignancy (carcinoma, lymphoma), collagen disease (SLE, dermatomyositis), Wegener's granulomatosis and after vaccination (polio, BCG).

Q: What history should be taken?

A: As follows:

- History of drugs.
- Infections.
- Any malignancy.
- Collagen disease.

Q: What **investigations** should be done in erythema multiforme?

A: As follows:

- CBC.
- ASO titre.
- Anti-HSV 1, anti-mycoplasma antibody.
- Other investigations according to suspicion of causes.

Q: How to **treat**?

A: As follows:

- Offending drugs should be stopped.
- Symptomatic (IV fluid, antipyretic and antibiotic), local care of eyes and mouth.
- Treatment of primary cause.
- In severe cases of SJS: IV immunoglobulin can be given.
- Aciclovir (in herpes simplex infection).
- Steroid: Its use is controversial. However, it can be used and should be tapered rapidly because once skin loss occurs, it may aggravate morbidity and mortality due to immunosuppression.

Q: What is **bullous** lesion? What are the **causes** of bullous lesion of the skin?

A: Bullae is a circumscribed, fluid-filled elevation of skin more than 1 cm in diameter. **Causes** are:

1. Common causes are:
 - Erythema multiforme.
 - Pemphigus vulgaris.
 - Bullous pemphigoid.
 - Dermatitis herpetiformis.
2. Others:
 - Bullous impetigo.
 - Insect bite.
 - Congenital: epidermolysis bullosa.
 - Porphyria cutanea tarda.
 - Staphylococcal scalded skin syndrome (SSSS) and toxic epidermal necrolysis (TEN).
 - Diabetic bullous lesions of skin.

DERMATITIS HERPETIFORMIS

Instructions by the examiner:

- Look at here. What is your diagnosis?

Presentation of a Case:

- There are multiple grouped, symmetrical, erythematous, polymorphous, papular, papulo-vesicular, vesiculo-bullous or bullous, urticarial and excoriated skin lesion on the extensor surface of knee, elbow, buttock, scalp, upper back and sacrum.
- Multiple scratch marks indicating that lesions are pruritic.

My diagnosis is **Dermatitis herpetiformis**.

Q: What is the **commonest symptom**?

A: Severe itching.

Q: What is the **characteristic type** of lesion?

A: Group lesions, symmetrical and characteristic distribution in extensor surface.

Q: What **history** do you like to take and why?

A: Diarrhoea or malabsorption after taking gluten containing diet (oat, rye, wheat, barley). There may be Coeliac disease, 10% of them may have dermatitis herpetiformis.

Q: What are the **differential diagnoses**?

A: As follows:

- Drug reaction.
- Erythema multiforme.
- SLE.
- Pemphigus vulgaris.
- Bullous pemphigoid.
- Scabies.
- Contact dermatitis.
- Atopic dermatitis.



Dermatitis herpetiformis (knee)



Dermatitis herpetiformis
(bullous lesion)



Dermatitis herpetiformis (elbow)

N.B. Remember the following points:

- *Dermatitis herpetiformis is common in male and male to female ratio is 2:1.*
- *80% of patients have HLA B8/DRw3.*
- *Intake of iodide and gluten-containing diet may precipitate an attack.*
- *Can occur at any stage of adult life, rare in childhood.*
- *It may be recurrent.*
- *Oral mucosa is rarely involved (when bullae are numerous).*
- *Higher incidence of developing malignancy than in general population (small bowel lymphoma).*
- *Hypothyroidism may also occur.*
- *May not be any symptoms of malabsorption, but abnormal D-xylose absorption may be found in 70% patients.*
- *Almost all patients have partial villous atrophy in jejunal biopsy, even if no GIT symptoms are present.*

READ THE FOLLOWING TOPICS IN RELATION TO DERMATITIS HERPETIFORMIS

Q: What is **dermatitis herpetiformis**? What is the pathophysiology?

A: It is an autoimmune bullous lesion of skin that is associated with gluten sensitive enteropathy. It is caused by IgA deposition at dermoepidermal junction leading to neutrophil chemotaxis, cytokine and complement activation, which results in vesicle formation at the dermoepidermal junction.

Q: What **investigations** should be done in dermatitis herpetiformis?

A: As follows:

1. Skin biopsy shows:
 - Infiltration of neutrophils, eosinophils, fibrin at dermal papilla and sub-epidermal vesicle.
 - Direct immunofluorescence in normal skin biopsy (perilesional) shows granular IgA deposition alone or with C₃ at dermoepidermal junction with accentuation in dermal papillae (IgM and IgG are occasionally found).
2. Anti-endomysial and tissue transglutaminase antibody may be present in serum. Anti-reticulin antibody may be present.
3. Endoscopic biopsy from duodenojejunal flexure to diagnose Coeliac disease. There is:
 - Short and wide villi (partial villous atrophy).
 - Total flat mucosa (subtotal villous atrophy).
 - Reduced height of epithelial cells and increased plasma cells in lamina propria and intra-epithelial lymphocytes.
4. HLA-typing (HLA-B8 and HLA-DR3 are positive in 80% cases).
5. Therapeutic trial with dapsone may reduce itching.

Q: How to **treat** dermatitis herpetiformis?

A: As follows:

- Dapsone: 100 to 150 mg daily (start with 100 mg, increase the dose gradually). To be continued, may be life-long. Relapse may occur if the drug is stopped. Dramatic clinical response occurs in 72 hours (a therapeutic test) and itching reduces quickly. Dose is decreased gradually. Maintenance dose is 50 mg/day.
- Gluten free diet (avoid wheat, rye, oat and barley).
- Other drugs: Sulphapyridine, sulphasalazine, colchicine, tetracycline with nicotinamide.

Q: What are the **complications** of dapsone therapy?

A: As follows:

- Blood dyscrasia (such as haemolytic anaemia, agranulocytosis, methaemoglobinaemia).
- GIT upset.
- Hepatitis.
- Neuropathy.
- Skin rash or exfoliative dermatitis.

N.B. Dapsone should be avoided in glucose-6-phosphate dehydrogenase deficiency.

Q: What are the **associations** in dermatitis herpetiformis?

A: As follows:

- Coeliac disease.
- Malignancy (lymphoma).
- Thyroid disorder (hypothyroidism).

HERPES ZOSTER (SHINGLES)

Instructions by the examiner:

- Look at here. What are your finding? What is your diagnosis?

Presentation of a Case No. 1:

- There are multiple vesicles or pustules, papules and few crusted lesions (in thoracic or lumbar region), which have not crossed the midline.
- Few scabs are preset over the lesion.

My diagnosis is **Herpes zoster**.

Q: What is the cause?

A: It is due to reactivation of **varicella zoster virus** that lies dormant in dorsal root ganglion of sensory nerves, following chicken pox in childhood. Thoracic dermatome is commonly involved.



Herpes zoster



Herpes zoster (healed)



Herpes Zoster (shoulder)



Herpes zoster (thigh)

Q: What are the sites of lesion?

A: As follows:

- Dorsal root ganglia (when thoracic or lumbar dermatome is involved).
- Gasserian ganglia (trigeminal ganglia), in herpes zoster ophthalmicus.
- Geniculate ganglia (in Ramsay Hunt's syndrome).

Q: What is the percentage of involvement of dermatome?

A: As follows:

- Thoracic: 55%.
- Cranial: 20% (trigeminal nerve is commonly involved).
- Lumbar: 15%.
- Sacral: 5%.

Q: Why reactivation occurs?

A: As follows:

- Spontaneous.
- Immunocompromised state: multiple myeloma, malignancy (lymphoma, leukaemia), HIV infection, steroid and cytotoxic drug therapy.

Q: Who are the high risk groups for herpes zoster?

A: Elderly and immune-compromised patients are the high risk groups.

Q: What history do you like to take?

A: As follows:

- History of chicken pox in childhood.
- Immunocompromised disease (multiple myeloma, lymphoma, leukaemia).
- Diabetes mellitus.
- Drugs (steroid and cytotoxic drug).
- Radiotherapy.

Q: What are the presentations of herpes zoster?

A: As follows:

- Initially, burning discomfort or pain along the involvement of dermatome and dysaesthesia is present (when thoracic dermatome is involved on right side, it confuses with acute cholecystitis. If in right sided iliac fossa, confused with acute appendicitis).
- After 3 to 4 days, redness is followed by papule, vesicle or pustules (lesions occur in cluster). Later, crust formation occurs after few days.

Q: What investigations are done to detect herpes zoster?

A: Diagnosis is usually clinical. Investigations are rarely necessary.

- Raising antibody titre.
- Viral culture (44% positive).
- PCR (97% positive).
- Tzanck smear from vesicle (75% positive).
- Histopathology shows intra-epidermal vesicle with large swollen cells, called balloon cells.

Q: What are the complications of herpes zoster?

A: As follows:

- Post-herpetic neuralgia.
- Secondary infections: Meningo-encephalitis, myelitis and motor radiculopathy (in lumbar and brachial).
- Bowel and bladder dysfunction occurs, if sacral root is involved. Generalized herpes zoster (may occur in Hodgkin's lymphoma, leukaemia, HIV, bronchial carcinoma).
- In ophthalmic herpes: corneal ulcer and iritis may occur.
- Ramsay Hunt's syndrome.
- Pleurisy, myocarditis and hepatitis.
- Others: Phrenic nerve palsy, muscle wasting. Rarely, purpura and necrosis of the affected segments occur (purpura fulminans).

Q: How to treat herpes zoster?**A:** As follows:

1. Local treatment:
 - Antiseptic powder (povidone-iodine), drying solution, calamine lotion and local aciclovir cream.
 - Topical idoxuridine: 5% solution during the first 36 hours of eruption may help.
 - Local application of heat and gentle pressure may help.
2. Systemic:
 - Oral aciclovir, 800 mg, five times daily or valacyclovir, 1 gm 8 hourly or famciclovir, 500 mg TDS for 1 week.
 - In immune-compromised patient: IV aciclovir 10 mg/kg 8 hourly **plus** anti-varicella zoster immunoglobulin may be given.
 - In severe cases: prednisolone 30 to 60 mg/day may be given (it does not cause dissemination). Systemic steroid is contraindicated in immunocompromised host.
3. Interferon may help in limiting herpes zoster in patients with cancer.
4. A 4 week course with prednisolone may help to reduce post-herpetic neuralgia.

Q: How to treat post-herpetic neuralgia?**A:** It occurs in 10% cases, common in elderly.

- Gabapentin and amitriptyline (separately or in combination).
- Topical: 10% lidocaine gel or 5% lidocaine–prilocaine in patch may be given.
- If no response: transcutaneous nerve stimulation (TENS) may help.
- A 3 week course of prednisolone 40 to 60 mg/day, taper in 3 weeks may be given, if no contraindication.
- If no response and in severe cases: ablation of ganglia may be tried (permanent anaesthesia of that part may occur).
- Usually there is no response to analgesics. It may take long time to recover, even up to 2 years.

Q: What is Ramsay Hunt's syndrome?**A:** It is the herpes zoster of geniculate ganglia characterized by:

- Rash in the external auditory meatus and palate.
- Ipsilateral VIIth cranial nerve palsy (lower motor neuron).
- Ipsilateral loss of taste and buccal ulceration.

Presentation of a Case No. 2:

- Same lesion on the face (as described in case no. 1 above) along the distribution of the ophthalmic division of trigeminal nerve, does not cross the midline.
- There is redness and ulceration in the cornea (right or left eye).

My diagnosis is **Herpes zoster ophthalmicus**.

Q: Which nerve is commonly affected?**A:** It commonly involves ophthalmic (first) division of trigeminal nerve.



Herpes zoster ophthalmicus (left side)



Herpes zoster ophthalmicus (involving all 3 divisions of trigeminal nerve)



Herpes zoster ophthalmicus (left side)



Herpes zoster ophthalmicus (healed)

Q: What are the clinical features?

A: As follows:

1. Pain, tingling and numbness, redness around the eye followed by vesicular or pustular lesions up to the scalp, don't cross the mid line (other 2 branches of trigeminal nerve, maxillary and mandibular nerves are rarely involved).
2. Eye features are:
 - Mucopurulent conjunctivitis.
 - Episcleritis, scleritis or iritis.
 - Keratitis, corneal ulcer or panophthalmitis.
 - Pupillary distortion.
 - Occasionally, optic atrophy and visual loss.
 - Choroidoretinitis, secondary glaucoma and cicatricial lid scarring.

Q: How to treat?

A: As follows:

1. Local care of the eye:
 - Local 3% aciclovir ointment (five times daily) and idoxuridine 0.1% drop in eye.
 - Local antibiotic eye drop.
 - Eye protection using sterile pad.
 - Oral aciclovir, 800 mg, five times daily or valacyclovir, 1 gm 8 hourly or famciclovir, 500 mg TDS for 1 week.
2. Consult with an ophthalmologist.

Q: Which cranial nerves are involved in herpes zoster?

A: As follows:

- Trigeminal nerve (commonly ophthalmic division).
- Facial nerve.
- Vestibulo-cochlear nerve.

ACANTHOSIS NIGRICANS

Instructions by the examiner:

- Look at here. What is your finding? What is your diagnosis?

Presentation of a Case:

- There are brown (or black), velvety plaques of skin (thick and rugose-like warts) in axilla and neck.
- Also, thickening and pigmentation on the back of the neck.
- Mention, if present in other sites (back of knee, umbilicus etc.).

My diagnosis is **Acanthosis nigricans**.

(Rarely involves conjunctiva, buccal mucosa and lip when the lesion is extensive).

Q: What are the **other sites** do you like to see?

A: Limb flexures, also may be found around the umbilicus, nipple and groins which are symmetrically distributed.



Acanthosis nigricans
(axilla)



Acanthosis nigricans
(front of neck)



Acanthosis nigricans
(back of neck)



Acanthosis nigricans
(flexure of knee)

Q: What is **acanthosis nigricans**?

A: Acanthosis nigricans is a disorder of skin characterized by dark, thick, velvety skin in body folds and creases.

Q: What are the **causes** of acanthosis nigricans?

A: As follows:

1. In young patient, <40 years of age:
 - Obesity (commonest cause).
 - Insulin resistance.
 - Endocrine diseases (Cushing's syndrome, acromegaly, hypo and hyperthyroidism, polycystic ovary syndrome).
2. Above 40 years of age, it is commonly due to malignancy:
 - Carcinoma of stomach (common cause) and other GIT malignancies.
 - Bronchial carcinoma.
 - Lymphoma.
 - In female: carcinoma of uterus, ovary, breast.

N.B. Remember the following points:

- *Acanthosis nigricans can affect healthy people.*
- *May be genetically inherited.*
- *Common in people of African descent.*
- *Drugs such as human growth hormone, OCP, steroid, fusidic acid can cause acanthosis nigricans.*
- *Acanthosis nigricans may occur in various syndromes such as Bloom's syndrome, ataxia-telangiectasia and Morfan's syndrome (Mental retardation, pre- and post-natal overgrowth, remarkable face and acanthosis nigricans).*

Q: What is the relation between **acanthosis nigricans** and **malignancy**?

A: Acanthosis nigricans may occur before the development of malignancy in 18% or may parallel with malignancy in 60% and may follow malignancy in 22% cases. Remission occurs with cure of malignancy and worsens again with recurrence.

READ THE FOLLOWING TOPICS IN RELATION TO ACANTHOSIS NIGRICANS

Q: What are the **types** of acanthosis nigricans?

A: As follows:

- Type I: acanthosis nigricans associated with malignancy.
- Type II: familial acanthosis nigricans.
- Type III: acanthosis nigricans associated with other diseases (e.g., obesity, insulin resistant state and endocrinopathy).

Q: How to **treat** acanthosis nigricans?

A: As follows:

- Treatment of primary cause.
- Reduction of weight, if obese.
- Topical application such as etretinate, tretinoin, calcipotriol, urea and salicylic acid.
- CO₂, laser ablation and long pulse alexandrite laser therapy.

Q: What are the **dermatological manifestations** of malignancy?

A: As follows:

- Acanthosis nigricans.
- Dermatomyositis.
- Thrombophlebitis migrans (crops of tender nodules along the blood vessels), commonly associated with carcinoma of pancreas (body and tail).
- Ichthyosis.
- Tylosis (thickening of palm and sole and dysphagia).
- Exfoliative dermatitis.
- Erythema nodosum.
- Urticaria.

ICHTHYOSIS

Instructions by the examiner:

- Look at here. What is your finding? What is your diagnosis?
- Examine the patient's skin. Or, perform general examination of this patient.

Presentation of a Case:

- Skin is rough, thick and dry (mention the site). There are multiple fish-like scales at the same site.

My diagnosis is **Ichthyosis**.

Q: What is ichthyosis?

A: Ichthyosis is the dry and rough skin with persistent visible scaling, which may resemble fish scale. Ichthyosis is not a single disease, but a group of diseases in which homeostatic mechanism of epidermal cell kinetics or differentiation is altered, resulting in the clinical appearance of scale.

Q: What does ichthyosis indicate?

A: It may be secondary to underlying malignancy or other diseases or due to drugs. Detailed history including any familial history and physical examination should be done. If short history of recent onset, highly suggestive of underlying malignancy. Also may be severe in HIV or AIDS.

Q: What are the types of ichthyosis?

A: It may be congenital or inherited and acquired:

Congenital or inherited:

1. Major:

- Autosomal dominant: Ichthyosis vulgaris and bullous ichthyosiform erythroderma.
- Autosomal recessive: Lamellar ichthyosis and non-bullous congenital ichthyosiform erythroderma.
- X-linked ichthyosis.

2. Minor: Harlequin foetus and ichthyosis linearis circumflexa.

3. Syndromes: Refsum's syndrome, Rud syndrome and Sjögren–Larsson syndrome.

Acquired:

- Hodgkin's and non-Hodgkin's lymphoma, mycosis fungoides, multiple myeloma, leprosy, AIDS, dermatomyositis, SLE.
- Drugs: Nicotinic acid, triparanol, butyrophenones and clofazimine.
- Others: Sarcoidosis, hypothyroidism and nutritional deficiency.



Ichthyosis vulgaris



Ichthyosis vulgaris
(back)



Ichthyosis vulgaris
(face)



Ichthyosis vulgaris
(legs)

Q: How to treat ichthyosis?

A: As follows:

- Treatment of primary cause.
- Symptomatic treatment with lactic acid, 12% ammonium lactate lotion, 10% urea cream, topical calcipotriene.

PEMPHIGUS VULGARIS

Instructions by the examiner:

- Look at here. What is your finding? What is your diagnosis?
- Examine the patient's skin. Perform general examination of this patient.

Presentation of a Case:

- There are multiple thin-walled blisters or bullae filled with clear fluid in the trunk, axilla and face.
- Some blisters are burst with ulcer and crust formation in erythematous base with oozing and bleeding.
- Multiple ulcers with some healed lesions are present.

My diagnosis is **Pemphigus vulgaris**.

Q: What are your differential diagnoses?

A: As follows:

- Bullous pemphigoid.
- Stevens–Johnson syndrome.
- Exfoliative dermatitis.

Q: What is the site of lesion in pemphigus vulgaris?

A: In the epidermis (above the basal layer).

Q: What is pemphigus vulgaris?

A: It is an autoimmune blistering disease characterized by thin-walled, flaccid, easily ruptured bullae that appear in apparently normal skin and mucous membrane or on erythematous base (associated with mouth ulcer).

Q: What are the causes of pemphigus vulgaris?

A: Exact aetiology is unknown. Probable factors are:

- Autoimmunity, as suggested by the intercellular deposition of IgG and C3 complement in epidermis.
- Genetic predisposition (associated with HLA DR4 and DR6).
- Drugs (penicillin, penicillamine, captopril, rifampicin, cephalosporin, pyrazolone).
- UV light, PUVA and ionizing radiation.
- Increased incidence in myasthenia gravis and thymoma.

Q: What are the types of pemphigus?

A: As follows:

- Pemphigus vulgaris.
- Pemphigus foliaceus.
- Paraneoplastic pemphigus.
- IgA pemphigus.

Q: What are the presentations of pemphigus vulgaris?

A: It is common in middle age, 50 to 60 years, equally in both sexes. Patient usually presents with:

- Thin-walled flaccid bullae, which easily rupture, causing erosion, ulcer and crust formation with oozing and bleeding.
- Mouth ulcer is common (in 60%), also conjunctival and genital ulcer may be present.
- Ulcer heals slowly with hyperpigmented patch without scarring.



Pemphigus vulgaris (thigh)



Pemphigus vulgaris (back)



Pemphigus vulgaris (mouth ulcer)

Q: What is the bedside test in pemphigus vulgaris?

A: As follows:

- Nikolsky's sign: Rubbing of uninvolved skin results in separation of epidermis from basal layer, called Nikolsky's sign.
- Bullae spread phenomenon or Asboe-Hansen sign: when pressure is put on the top of the bulla, there is extension of blister into the adjacent unblistered skin.

Q: What are the causes of Nikolsky's sign?

A: As follows:

- Pemphigus vulgaris (common cause).
- Pemphigus foliaceus.
- Toxic epidermal necrolysis (TEN).
- Staphylococcal scalded skin syndrome (SSSS).
- Epidermolysis bullosa (dystrophic type).

Q: What investigations should be done in pemphigus vulgaris?

A: As follows:

1. Routine:
 - CBC.
 - Blood sugar.
 - Urine RME.
 - Liver function tests.
 - Renal function tests.
2. Definitive:
 - **Skin biopsy** for histopathology and immunofluorescence test (an early intact bullae <12 hours duration should be taken with perilesional area).
 - Cytological (**Tzanck method**): Smears are taken from the base of a bulla and is used for rapid demonstration of acantholytic cell (using Giemsa stain, which shows no intercellular bridge, darkly staining cytoplasm and large nuclei surrounded by lightly staining halo).
 - **Direct immunofluorescence** shows intercellular deposition of IgG throughout epidermis (both involved and normal skin) or oral mucosa and C3 deposition in acantholytic area (net-like, honey-comb or mosaic pattern).

Histological findings:

- Acantholysis (separation of individual keratinocyte from one another).
- Superficial intra-epidermal split.

- Intra-epidermal blister above basal layer (in pemphigus vulgaris) or subcorneal epidermal split (in pemphigus foliaceus).
- Acantholytic cells are found lining the bulla as well as lying free in the bulla cavity.
- Eosinophilic spongiosis and occasionally neutrophilic spongiosis may be seen in the spongiotic epidermis in pemphigus vulgaris.

Q: How biopsy and DIF materials are collected?

A: As follows:

- A small early intact bulla should be taken. Site of biopsy is frozen with aerosol refrigerant spray so that the punch may include firm tissue. Tissue for biopsy is taken in test tube containing formalin.
- Normal appearing perilesional skin is taken in saline soaked gauze for DIF.

Q: What is the prognosis?

A: Prognosis is bad, recurrence is common with high mortality.

Q: What are the complications of pemphigus vulgaris?

A: As follows:

- Secondary bacterial infection (pneumonia, septicaemia).
- Hypoproteinaemia.
- Side effects of systemic prednisolone.

Q: How would you treat the patient?

A: As follows:

1. General measures:
 - Bed rest.
 - Daily bath to remove thick crusts and foul odour.
 - Maintenance of fluid and electrolyte balance.
 - Maintenance of nutrition.
 - Antibiotic, if secondary infection.
 - Blood transfusion (if necessary).
2. Topical:
 - 1% silver sulfadiazine is applied topically.
 - Antiseptic mouth wash and viscous xylocaine are applied in the mouth.
 - Care of the eye.
3. Systemic:
 - High dose prednisolone 100 to 200 mg/day,
 - When remission occurs with no new blister, tapering of steroid.
 - Maintenance dose is given for long time (may require life-long). If new blister occurs during treatment, dose of prednisolone should be increased.
4. Other treatment:
 - IV methylprednisolone 1 g/day for 5 days (pulse therapy).
 - Mycophenolate mofetil 1 to 1.5 gm is given twice a day (commonly used as steroid sparing drug).
 - Other drugs: Azathioprine, cyclophosphamide, methotrexate, cyclosporine and dapsone.
 - In resistant case: IV immunoglobulin may be tried.
 - Biologic agents: monoclonal anti-CD20 antibody (rituximab), anti-TNF α (infliximab and etanercept) may be given.
 - Extra-corporeal photochemotherapy.

PEMPHIGOID (BULLOUS)

Instructions by the examiner:

- Look at here. What are your findings? Or examine the skin of this patient.

Presentation of a Case:

- There are multiple tense, unruptured bullae with clear or haemorrhagic fluid, present in the trunk, axilla and limbs.
- No mouth ulcer.

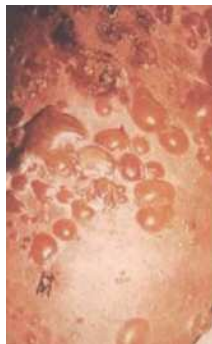
My diagnosis is **Bullous pemphigoid**.

Q: What is the site of lesion in pemphigoid?

A: In the basement membrane between epidermis and dermis (**sub-epidermal**), hence less tendency to rupture.



Bullous pemphigoid



Bullous pemphigoid



Bullous pemphigoid



Pemphigus vulgaris
(ruptured bullae)

Q: What are your differential diagnoses?

A: As follows:

- Pemphigus vulgaris.
- Dermatitis herpetiformis.
- Stevens–Johnson syndrome.
- Toxic epidermal necrolysis (TEN).

Q: What investigations do you suggest?

A: As follows:

1. Routine:
 - CBC.
 - Blood sugar.
 - Urine R/M/E.
2. Confirmatory:
 - Tzanck test.
 - Skin biopsy for histopathology and DIF.

Q:How to **confirm** the diagnosis of bullous pemphigoid?

A: Skin biopsy for histopathology and direct immunofluorescence shows deposition of IgG and complement C3 at the basement membrane (in a linear pattern). Histopathological findings are:

- Sub-epidermal bullae.
- Absence of acantholysis.
- Superficial dermal infiltration of many eosinophils.

Q:What is **bullous pemphigoid**?

A: It is an autoimmune blistering disease characterized by tense bulla, not associated with mouth ulcer. It is associated with IgG autoantibodies directed against antigen BP230 (BP Ag1) and BP180 (BP Ag2), deposited at basement membrane between epidermis and dermis.

Q:What are the **presentations or clinical features** of pemphigoid?

A: It is common in elderly, >60 years. The patient presents with:

- Tense bullae, less rupture, with a tendency to heal, may be red urticarial patch, mostly in trunk, limbs and flexures.
- Usually no mouth involvement (may involved rarely, in <20%).

N.B. Pemphigoid may be associated with lymphoma.

Q:How to **treat** bullous pemphigoid?

A: As follows:

1. General treatment: Bed rest, maintenance of electrolyte, adequate nutrition etc.
2. Steroid:
 - Prednisolone 0.5 to 0.75 mg/kg/day, should be tapered slowly over few weeks after clinical improvement (may be required to continue for 2 to 3 years).
 - Potent topical steroid can be given alone.
 - In severe cases: methylprednisolone, IV daily for 3 to 5 days.
3. Tetracycline 500 mg 6 hourly with nicotinamide 500 mg 8 hourly.
4. Other drugs: dapsone, azathioprine, methotrexate, cyclophosphamide, cyclosporine and mycophenolate mofetil.
5. IV immunoglobulin.
6. Antihistamine, if needed.

N.B. Bullous pemphigoid responds to lower dose of prednisolone.

Q:What are the **causes** of bullous lesion in skin with mouth ulcer?

A: As follows:

- Pemphigus vulgaris.
- Stevens–Johnson syndrome.
- Toxic epidermal necrolysis.
- Behçet’s syndrome.
- SLE.

Q: What are the **differences between pemphigus vulgaris and bullous pemphigoid?**

A: As follows:

Points	Pemphigus Vulgaris	Bullous Pemphigoid
1. Age	Middle age (50 to 60 years).	Elderly (>60 years).
2. Distribution	Scalp, face, flexures, may be generalized.	Trunk, limb, flexures.
3. Mucosa of mouth, conjunctiva & genitalia	Commonly involved.	Usually not involved.
4. Lesion	Intra-epidermal, flaccid bullae, rupture easily and less tendency to heal.	Sub-epidermal, large, tense bullae, do not rupture easily and more tendency to heal.
5. Nikolsky's signs & Asboe-Hansen signs	Positive.	Negative.
6. Target antigen	Desmoglein 3, sometimes desmoglein 1	BP 230 and BP 180.
7. Antigens (kDa)	130 kDa and 160 kDa.	230 kDa and 180 kDa.
8. Direct immuno-fluorescence	Intercellular deposition of IgG and C3 in mosaic pattern (C3 only lesional).	Basement membrane deposition of IgG and C3 in linear pattern (C3 both lesional and non lesional).
9. Treatment	High dose steroid.	Low dose steroid.
10. Prognosis	Bad.	Better.

ARSENICOSIS (CHRONIC ARSENIC TOXICITY)

Instructions by the examiner:

- Look at here, what is your diagnosis? Examine the skin of the patient. Or, perform general examination.

Presentation of a Case No. 1: (By Looking of the Trunk and Abdomen).

- There are multiple hyperpigmented areas (mention the site), with scattered hypopigmented area giving rise to rain drop appearance.

My diagnosis is **Chronic arsenic toxicity (arsenicosis)**.

Q: What else do you want to examine?

A: I want to examine the palm and sole.

Presentation of case No. 2: (By General Examination).

- As above. **Plus**
- Multiple hard papular and plaque-like lesions with hyperpigmentation involving . . . (mention the site).
- Hyperkeratosis of palm and sole (rough and thick).

My diagnosis is **Chronic arsenic toxicity**.

Q: What are the differential diagnoses?

A: As follows:

1. For pigmentation:
 - Lepromatous leprosy.
 - Haemochromatosis.
 - Addison's disease.
 - Xeroderma pigmentosum.
 - Guttate psoriasis.
 - Tinea versicolor.
 - Idiopathic guttate hypomelanosis.
 - Post-inflammatory hypopigmentation and hyperpigmentation.
 - Drug melanosis.
2. For keratosis:
 - Epidermodysplasia verruciformis.
 - Multiple corn or callosities.
 - Verruca vulgaris.
 - Hereditary palmoplantar keratoderma.
 - Acrokeratosis verruciformis.

Q: What is the mechanism of arsenic toxicity?

A: After absorption, arsenic is widely distributed to all the tissues of the body. It combines with sulphhydryl-containing substances and inhibits the activity of many enzymes. It also interferes with cell enzymes, cell respiration and mitosis.



Hyperkeratosis of palm



Hyperkeratosis of sole



Raindrop pigmentation



Hyperpigmentation with scaly lesions

Q: What are the clinical presentations of arsenicosis?

A: As follows:

- Melanosis: Hyperpigmentation (generalized or localized) with few scattered hypopigmented areas giving rise to **raindrop** appearance.
- Hyperkeratosis of palm and sole. May be multiple, punctate, hard, discrete, papule and verrucous plaque.
- Nails: Brittle, may show transverse white striae of finger nails (called **Mee's line**).
- Hair: Dry, may fall off.
- Eye: Conjunctivitis.
- Nose: Rhinitis, epistaxis, nasal obstruction and septal perforation.
- It may involve any system of the body (liver, kidney, lung and heart).

Q: What are the diagnostic signs of arsenicosis?

A: As follows:

- Hyperkeratosis of palm and sole.
- Hyperpigmentation and hypopigmentation (on trunk and extremities) are the hallmarks.

Q: What are the systemic effects of chronic arsenic toxicity?

A: As follows:

- GIT: Anorexia, nausea and vomiting.
- Hepatic: Hepatomegaly, cirrhosis of liver and non-cirrhotic portal hypertension.
- Central nervous system: Peripheral neuropathy, seizure, confusion and encephalopathy.
- Haematological: Anaemia, leucopenia and thrombocytopenia.
- Musculoskeletal: Myalgia, arthralgia and atrophy of extensor muscles, causing wrist drop or foot drop.
- Renal: Dysuria, anuria and renal tubular necrosis.
- Heart: Cardiomyopathy, dysrhythmia and heart failure.
- Vascular: Peripheral vascular insufficiency, causing black foot disease.
- Endocrine: Diabetes mellitus may be precipitated.
- Malignancy: Skin (Squamous cell carcinoma, basal cell carcinoma and Bowen's disease), Carcinoma of lung, kidney, urinary bladder, liver (angiosarcoma), prostate and colon.

Q: How to **confirm** chronic arsenic poisoning?**A:** By measuring the arsenic concentration in hair, nail, urine and serum.**Normal value of arsenic:**

- Blood: <3 mg/L (or 5 to 50 ppb/mg/L).
- Urine: 0.005 to 0.04 mg/L.
- Hair: 0.08 to 0.25 mg/kg (pubic hair is preferred due to lack of contamination).
- Nail: 0.43 to 1.08 mg/kg.
- Daily urinary excretion: <0.1 mg/L.

N.B. Remember the following points:

- *Skin manifestation may require 1 year to develop.*
- *Systemic manifestations may require 10 years to develop.*
- *Early signs of arsenic toxicity: Conjunctivitis, transient icterus and hyperhidrosis.*

Q: What other **investigations** should be done in chronic arsenic toxicity?**A:** As follows:

- CBC.
- Urine R/M/E.
- Chest x-ray.
- Liver function tests.
- Renal function tests.
- ECG.
- EEG.
- Nerve conduction test.
- Other investigations according to organ involvement.

Q: How to **treat** chronic arsenic toxicity?**A:** As follows:

1. Drinking of arsenic contaminated water must be stopped.
2. High protein diet.
3. Antioxidant (vitamin A 50,000 IU, vitamin C 500 mg and vitamin E 200 mg daily for 3 months).
4. Vitamins and minerals supplement.
5. Vegetables and fresh fruits.
6. *Spirulina* (an algae), which is rich in high protein, may help to clear arsenic.
7. For skin lesion: Keratolytic emollients (salicylic acid, urea and retinoic acid), cryotherapy, electrocautery and laser therapy.
8. Drugs (chelating agent may be used):
 - D-penicillamine (250 mg TDS) for 3 months, or
 - Dimercaprol (BAL), dimercaptosuccinic acid (DMSA) and dimercapto-propane-sulphonate (DMPS). BAL has a tendency to redistribute arsenic to brain and testes. DMSA and DMPS are more preferable because of their low toxicity.

Dose: As follows:

- DMSA 10 mg/kg/day for 7 days followed by 10 mg/kg/day three times for 14 days.
- DMPS: 100 mg TDS to QDS for every alternate week for three courses.

Preventive therapy: Drinking water should be safe.

SCABIES

Instructions by the examiner:

- Look at here. What is your diagnosis? Or, perform the general examination.

Presentation of a Case:

- There are multiple erythematous, excoriated papules, vesicles, pustules and scratch marks involving the interdigital area, fingers, ulnar edge of the hand and anterior part of the wrist.

My diagnosis is **Scabies**.

Q: What are sites of scabies?

A: Commonly interdigital area, fingers, ulnar edge of hand, wrist. Other sites are antecubital fossa, elbow joint, axilla, areola, around umbilicus, lower abdomen, genitalia, buttock and dorsum of foot (face and scalp are never involved except in infants, children and immuno-compromised).

Q: What is the causative organism?

A: *Sarcoptes scabiei hominis*.



Scabies (hand)



Scabies (in genitalia)



Infected scabies



Burrow in scabies

Q: What are the modes of transmission of scabies?

A: Direct skin contact from the affected patient. Also from contaminated bed sheet or clothes.

Q: What are the clinical presentations of scabies?

A: As follows:

- Intense itching, mostly at night. Associated secondary infection may be present (called infected scabies).
- Papular lesions, excoriations and burrows at the sites of predilection.
- Presence of same features among family members or close associates.
- In women, itching of nipple associated with generalized pruritic papular eruption.
- In men, itchy papules in scrotum and penis.
- The patient may present with typical classical features or atypical form or features of complication.

Q: What is the diagnostic sign of scabies?

A: Burrow, which is short, wavy, dirty appearing line, found in the edge of fingers, toes or at the sides of hand and foot. Burrow contains female mites, eggs and faeces of the mite.

Q: How to diagnose scabies?**A:** As follows:

- Usually clinical (hand lens is used to see burrow and mite).
- Microscopical examination by scraping from lesion to see the mites.

Q: What are the differential diagnoses of scabies?**A:** As follows:

- Papular urticaria.
- Atopic dermatitis.
- Dermatitis herpetiformis.
- Pityriasis rosea.
- Pediculosis corporis.

Q: What are the types of scabies?**A:** As follows:

1. Classical scabies.
2. Others:
 - Scabies in a clean person.
 - Scabies incognito.
 - Nodular scabies (pink, tan, brown or red nodules can be seen, from 2 to 20 mm in diameter). The mite is not present in the nodular lesion.
 - Crusted scabies (Norwegian): Atypical form, common in immuno-compromised and institutionalized population. Lesion may be hyperkeratotic and crusted. Scaling is common and pruritus may be less.
 - Bullous scabies.

Q: What are the complications of scabies?**A:** As follows:

- Secondary bacterial infection.
- Eczematization and lichenification.
- Post-streptococcal glomerulonephritis.
- Others: Urticaria, exfoliative dermatitis, acrophobia and vasculitis.

Q: How to treat scabies?**A:** As follows:

1. Drugs:
 - Permethrin 5% cream: Single application (from neck to toe) may be repeated after 1 week.
 - 1% gamma benzene hexachloride lotion.
 - Benzyl benzoate 25% lotion (apply for consecutive 3 nights).
 - Monosulphiram 5 to 8% emulsion (apply for consecutive 3 nights).
 - 10% precipitated sulphur in white petrolatum (apply for consecutive 3 nights).
 - Crotamiton 10% lotion or cream.
 - Ivermectin may be helpful in immune-compromised, crusted or Norwegian scabies (200 mg/kg in single dose).
 - Ivermectin orally can be used in cases where topical therapy is difficult or impractical (e.g., widespread infestations in nursing homes).
 - Scabetic nodules may require intranodular corticosteroid injection.

2. General measures:

- Control of secondary infection.
- For itching: antihistamine.
- Scrub bath before the application of topical medicine.
- Washing of the cloths and bed sheet.
- Simultaneous treatment of the affected family members.

Q: What are the causes of **treatment failure** in scabies?

A: As follows:

- Improper dilution of topical medicine.
- Faulty method of application.
- Scrub bath not taken.
- Secondary bacterial infection is not controlled.
- Clothes and bed sheets are not properly sanitized.
- If simultaneous treatment is not given to other affected members of the family.
- If personal hygiene is not properly maintained.

LUPUS VULGARIS

Instructions by the examiner:

- Look at face. What is your diagnosis? What are the possible differential diagnoses?

Presentation of a Case:

- There is reddish-brown plaque (or nodules) with irregular margin in the right (or left) side of the face, surface is smooth and glistening with fine scaling over it.
- Non-tender, soft in consistency with atrophic scar in one place and spread in other.

My diagnosis is **Lupus vulgaris**.

Q: What are the differential diagnoses?

A: As follows:

- Sarcoidosis.
- Cutaneous leishmaniasis.
- Leprosy.
- Discoid lupus erythematosus (DLE).
- Dermatomyositis.
- Psoriasis.
- Rosacea.
- Deep mycosis.
- Wegener's granulomatosis.
- Bowen's disease.
- Lymphocytoma.



Lupus vulgaris
(plaque form)



Lupus vulgaris
(papular form)



Lupus vulgaris
(ulcerative)



Lupus vulgaris
(ulcerative)

Q: What is lupus vulgaris?

A: It is a cutaneous tuberculosis occurring in a person with moderate or high degree of immunity, as a post-primary infection.

Q: What are the common sites?

A: It commonly involves the skin of head and neck in 80% cases, particularly seen around the nose, also in arms and legs (in India, buttock and trunk are commonly involved). The lesion looks like apple-jelly, when seen by a glass slide pressed over it. Lesions heal with scarring and new lesions slowly spread out to form a chronic solitary erythematous plaque. Chronic lesions are at high risk of developing squamous cell carcinoma.

Q: What are the usual features of lupus vulgaris?

A: The lesion starts as a small enlarging red-brown papule. Multiple papules may occur, coalesce to form a slowly growing plaque with thickened and hyperkeratotic margin with central atrophy. Scarring is a characteristic feature.

Q: What are the complications of lupus vulgaris?

A: Squamous cell carcinoma, basal cell carcinoma.

Q: What are the clinical types of lupus vulgaris?

A: 5 types:

- Plaque form.
- Ulcerative and mutilating form.
- Vegetating form.
- Tumour-like form.
- Papular and nodular form.

Q: What are the types of cutaneous TB?

A: According to the source of infection, 4 categories of cutaneous TB:

1. Inoculation TB (exogenous source):
 - Primary inoculation complex.
 - TB chancre.
 - Warty TB (verrucous cutis).
 - Some lupus vulgaris.
2. Secondary TB (endogenous source):
 - Contiguous spread: Scrofuloderma.
 - Auto-inoculation: TB orofacialis.
3. Haematogenous spread:
 - Some lupus vulgaris.
 - Acute miliary TB.
 - Tuberculous ulcer.
 - Gumma or abscess.
4. Eruptive TB (tuberculids):
 - Micropapular: Lichen scrofulosorum.
 - Papular: Papular or papulo-necrotic tuberculid.
 - Nodular: Erythema induratum (also called Bazin's disease).

Q: What are the atypical mycobacteria causing cutaneous TB?

A: As follows:

- *Mycobacterium marinum* (responsible for swimming pool granuloma. It is found in swimming pool, lagoon or lake).
- Others are *M. scrofulaceum*, *M. gordonae*, *M. szulgai*, *M. avium-intracellulare* complex, *M. haemophilum*, *M. chelonae* and *M. ulcerans* (causes Buruli ulcer).

Q: What is the relationship of lupus vulgaris with TB in other organs?

A: As follows:

- 46% have tuberculous lymphadenitis.
- 15 to 20% have pulmonary TB and TB of bones and joints.

Q: What is the **pathogenesis** or **mode of infection** in lupus vulgaris?

A: As follows:

- It commonly occurs in normal skin, at the site of inoculation.
- Direct extension from underlying infected gland or joints.
- Lymphatic spread from mucous membrane of nose and throat.
- Haematogenous spread from other site.
- At the site of primary inoculation, also BCG vaccination or in the scar of scrofuloderma.

Organisms may remain latent in the skin for many years. Local trauma, non-specific inflammatory change or immuno-compromised disorder may be responsible for reactivation of cutaneous TB.

Q: How to **investigate**?

A: As follows:

- CBC and ESR.
- Mantoux test.
- Chest x-ray.
- Skin biopsy for histopathology.

Q: How to **treat**?

A: Standard anti-tubercular therapy should be given:

- 4 drugs for initial 2 months.
- In continuation phase, 10 months.

LICHEN PLANUS

Instructions by the examiner:

- Look at here. What is your diagnosis? Or, perform general examination of this patient.

Presentation of a Case:

- This patient has flat-topped, pruritic and polygonal violaceous papules on the flexors of wrist, trunk, medial aspect of thighs and shins.
- Wickham striae and Koebner's phenomenon are present (mention, if any).
- Oral mucosa shows reticulated whitish (or violaceous) plaques with pin-head papules in the inner side of cheeks.
- Nail shows longitudinal grooving, proximal and distal onycholysis, ridging and splitting.

My diagnosis is **Lichen planus**.

Q: What are the **other causes** of flat topped papules?

A: As follows:

- Lichen amyloidosis.
- Lichen nitidus.
- Lichen myxoedematosus.

Q: What is the **cause** of Wickham striae?

A: It is due to focal increase in thickness of granular layer and epidermis, better seen with hand lens (and by aniline dye).

Q: What are the **types** of mucosal lesions?

A: As follows:

- Ulcerative: 50%.
- Reticulate: 30%.
- Atrophic: 20%.



Lupus vulgaris
(plaque form)



Lichen planus (toes)



Lichen planus
(leg and foot)



Lichen planus (mouth)

Q: What are the **causes** of lichen planus?

A: As follows:

- Idiopathic.
- Drugs.
- Hepatitis C infection predisposes to lichen planus.

Q: What are the **drugs** that may cause lichenoid drug reaction?

A: β -Blockers, thiazides, spironolactone, frusemide, ACE inhibitors, calcium channel blockers, antimalarials, heavy metals, arsenic, lithium, iodides.

Q: How would you **differentiate** between lichenoid drug reaction and lichen planus?

A: As follows:

Points	Lichen Drug Reaction	Lichen Planus
1. Site	Sun-exposed areas	Flexor areas
2. Lesions	Larger and scaly	Smaller
3. Wickham striae	Absent	Present
4. Alopecia	More	Less
5. Mucosal involvement	Less	More

Q: What are the **types** of lichen planus?

A: As follows:

1. Morphological type:
 - Annular.
 - Linear.
 - Hypertrophic.
 - Atrophic.
 - Vesico-bullous.
 - Ulcerative and erosive.
 - Actinic.
 - Follicular.
 - Lichen planus pigmentosus.
 - Guttate and perforating.
2. Special variants:
 - Lichenoid drug reaction.
 - Lichen planus pemphigoides.
 - Lichen planus and LE overlap.
 - Keratosis lichenoides chronica.
 - Lichen planus and malignant transformation.
 - Lichen planus and hepatitis C association.
 - Lichenoid reaction of graft versus host disease.

Q: What are the **differences** between lichen planus and lichen nitidus?

Points	Lichen Planus	Lichen Nitidus
1. Size	Variable, usually large	1–2 mm
2. Shape	Polygonal	Round
3. Colour	Erythematous to violaceous	Shiny and discrete
4. Wickham striae	Present	Absent
5. Pruritus	Marked	Uncommon
6. Mucosal change	Frequently present	Rare

Q: What are the **differential diagnoses** of lichen planus?

A: Differential diagnoses of lichen planus depends on the type.

1. Hypertrophic:
 - Lichen simplex chronicus.
 - Psoriasis.
 - Lichen amyloidosis.
2. Annular:
 - Granuloma annulare.
 - Annular syphilis.
 - Annular psoriasis.
3. Linear:
 - Lichen striatus.
 - Linear morphoea.
4. Atrophic:
 - Lichen sclerosus et atrophicus.
 - DLE.
5. Guttate:
 - Guttate psoriasis.
 - Pityriasis rosea.
6. Oral:
 - Candidiasis.
 - Secondary syphilis.
7. Follicular:
 - Lichen spinulosus,
 - SLE.

Q: What **investigations** should be done in lichen planus?

A: As follows:

- CBC.
- Viral marker for hepatitis B and C.
- Skin biopsy for histopathology and DIF.
- Liver function tests and renal function tests (for therapeutic purpose).

Q: What are the histopathological and DIF findings in lichen planus?**A:** As follows:

- Histopathology shows hyperkeratosis, beaded hypergranulosis and saw-tooth pattern of epidermal hyperplasia. There is destruction of basal layer, which is squamatized. In superficial dermis, there is dense band-like infiltration of lymphocytes and melanophages. Civatte bodies represent necrotic keratinocytes.
- DIF shows clumps of IgM and less frequently IgA, IgG and C₃ sub-epidermally corresponding to Civatte bodies.

Q: How to treat lichen planus?**A:** Treatment depends on the type and extent of the disease:

1. General measures:
 - Avoid drugs like diuretics, β -blockers and antimalarials.
 - Protection from trauma.
2. Cutaneous lesions:
 - Topical steroid and sometimes intra-lesional steroid.
 - Systemic therapy: In widespread lesions, systemic steroid 1 mg/kg/day for 7 days, then taper (40 mg for 7 days and 20 mg for 7 days).
 - Narrow-band UVB and PUVA.
 - Isotretinoin and acitretin (0.5 to 1 mg/kg/day).
 - Cyclosporine.
 - Mycophenolate mofetil.
3. Oral lesions:
 - Topical steroid in orabase, nystatin with clobetasol, topical tretinoin with steroid and 0.1% topical tacrolimus.
 - PUVA and 308 nm excimer laser.
 - Systemic: Hydroxychloroquine 200 to 400 mg/day for 6 months. Thalidomide 150 mg/day.
 - Other agents used in cutaneous lesions also improve oral lesions.

Q: What is the course or prognosis of lichen planus?**A:** Two-thirds patients will have lichen planus of less than 1 year. Many patients are cured spontaneously within 1 year. Recurrence occurs in half of the patients.**Q: What are the medical causes of itching?****A:** As follows:

1. Liver disease: Primary biliary cirrhosis, obstructive jaundice.
2. Chronic renal failure.
3. Haematological: Polycythaemia rubra vera (after warm bath), lymphoma (especially Hodgkin's disease), leukaemia, multiple myeloma, iron deficiency anaemia.
4. Endocrine cause: Hypothyroidism, thyrotoxicosis, diabetes mellitus (especially associated with candidiasis).
5. Any internal malignancy.
6. HIV.
7. Psychogenic.

EXFOLIATIVE DERMATITIS

Instructions by the examiner:

- Look at here. What is your diagnosis? Or perform the general examination of this patient.

Presentation of a Case:

- The patient has generalized exfoliation and erythema involving different parts of the body (mention the site). There is also oozing of serosanguinous fluid.
- Skin is dry and warm.
- Nails are brittle, yellowish with subungual hyperkeratosis, onycholysis and dystrophy.

My diagnosis is **Exfoliative dermatitis**.

Q: What are the **clinical features** of exfoliative dermatitis?

A: As follows:

1. Cutaneous manifestations:

- Extensive exfoliation, scaling covering more than 90% of body surface and pruritus with widespread erythema.
- Skin thickening and loss of hair (often).
- Nails may be dystrophic.
- Palms and soles are involved, mucous membranes are usually spared, but mucous membrane of upper respiratory tract and conjunctiva may be involved.

2. Systemic manifestations:

- Diarrhoea.
- Anaemia, oedema and tachycardia.
- Lymphadenopathy (due to reactive hyperplasia).
- Hepatomegaly (in 7 to 37% cases).
- Splenomegaly (in 3 to 23% cases).
- Occasionally, gynaecomastia.



Exfoliative dermatitis
in psoriasis



Erythroderma



Exfoliative dermatitis
(hand)



Exfoliative dermatitis
(legs)

Q: What are the causes of erythroderma in childhood?**A:** As follows:

- Atopic dermatitis.
- Leiner's disease.
- Bullous ichthyosiform erythroderma and non-bullous ichthyosiform erythroderma.
- Lamellar ichthyosis.
- Pityriasis rubra pilaris.
- Idiopathic.
- Drugs.
- Generalized dermatophytosis.
- Leukaemia.
- Childhood dermatomyositis.

Q: What are the causes of erythroderma in adults?**A:** Primary or idiopathic and secondary to other disease. Causes are:

1. Cutaneous disease:
 - Psoriasis.
 - Atopic dermatitis.
 - Neurodermatitis.
 - Dermatophytosis.
 - Contact dermatitis.
 - Seborrhoeic dermatitis.
 - Stasis dermatitis.
 - Pityriasis rubra pilaris.
 - Pemphigus foliaceus.
2. Systemic disease:
 - Lymphoma.
 - Leukaemia.
 - Carcinoma (of lung, rectum, other malignancy).
 - Multiple myeloma.
 - HIV infection.
 - Graft versus host disease.
3. Drugs: Barbiturate, carbamazepine, dapsone, sulphonamide, allopurinol, lithium, phenothiazines, thiazide.

Q: What is the pathogenesis of exfoliative dermatitis?

A: There is increased rate of epidermal turn over. The number of germinative cells and their absolute mitotic rate are increased. Transit time of the cells through epidermis is shortened. Consequently, more material is lost from the epidermis. Desquamated cells show increased amount of nucleic acids and their degenerative products, decreased amount of free amino acids and increased amount of soluble protein.

Q: What are the causes of exfoliative dermatitis with nail changes?**A:** As follows:

- Psoriasis.
- Pityriasis rubra pilaris.
- Lichen planus.
- Dermatophytosis.
- Atopic dermatitis.

Q: What investigations should be done in erythroderma?**A:** As follows:

1. CBC: Normochromic normocytic anaemia, leucocytosis, eosinophilia and ESR (high).
2. Urine (proteinuria).
3. Chest x-ray (to see pneumonia, lymphoma, sarcoidosis and carcinoma).
4. Total protein and A/G ratio (hypoproteinaemia, altered A/G ratio).
5. Serum IgE (high in some cases, e.g., atopic dermatitis).
6. Serum electrolytes (hypokalaemia and hyponatraemia).
7. Others (according to the suspicion of causes):
 - Skin biopsy for histopathology and DIF.
 - Skin scraping for fungus and fungal culture (in dermatophytosis).
 - ECG and echocardiogram in suspected cases of heart failure.
 - Bone marrow examination (to exclude leukaemia and myeloma, secondary deposits).
 - USG of whole abdomen.
 - Test for HIV.
 - CT scan and MRI, if needed.

Q: What are the causes of hypoproteinaemia in exfoliative dermatitis?**A:** As follows:

- Increased protein loss via scaling or leaking through the skin.
- Protein losing enteropathy.
- Decreased synthesis and increased catabolism of protein.
- Dilution by increased plasma volume.

Q: What are the complications of exfoliative dermatitis?**A:** As follows:

1. Metabolic:
 - Loss of permeability barrier causes xerosis, water loss and dehydration.
 - Marked scaling causes protein loss and hypoalbuminaemia.
 - Marked vaso-permeability causes oedema.
 - Marked vasodilatation causes chills, hypothermia and high output cardiac failure.
2. Other complications:
 - Secondary infection.
 - Electrolyte imbalance.
 - Dermatogenic enteropathy (diarrhoea).
 - Thrombophlebitis.

Q: How to treat?**A:** As follows:

- General measures: Maintenance of fluid and electrolyte balance, nutrition and protein balance by high-protein diet. Intake and output monitoring, maintenance of environmental temperature and frequent bathing.
- Emollients and lubricants: Liquid paraffin, vaseline and olive oil or 12% ammonium lactate.
- Symptomatic: Antibiotic to control infection, antihistamine to control pruritus and diuretics, if oedema and cardiac failure.
- In severe persistent cases: systemic steroid may be given (triamcinolone acetonide 80 mg IM as initial dose, repeated on fourth, seventh and tenth day according to the condition of the patient).
- Other drugs: Methotrexate, cyclosporine and acitretin can be used in psoriatic erythroderma. Isotretinoin can be used in erythroderma caused by pityriasis rubra pilaris. Immunosuppressives such as azathioprine and cyclophosphamide may be required occasionally.
- PUVA therapy can be used in mycosis fungoides or psoriasis.
- Treatment of primary causes (e.g., lymphoma or leukaemia).

N.B. If possible, systemic steroid should be avoided due to the dangers of fluid retention, secondary infection, diabetes and other complications. They should be avoided in psoriatic erythroderma for they may provoke development of pustular psoriasis. Steroid should be used cautiously in atopic and seborrhoeic dermatitis.

Q: What is the prognosis of exfoliative dermatitis?**A:** Depends on causes:

- Prognosis is good in drug-induced cases after the offending drug is withdrawn.
- Prognosis is poor in idiopathic erythroderma.
- For patients with psoriasis, atopic dermatitis or seborrhoeic dermatitis: it may continue for months, respond slowly and tend to relapse.
- For the patients with underlying diseases or malignancy: prognosis depends on the outcome and the course of the disease process.
- The mean duration of the disease is 5 years with a median of 10 months.
- The overall mortality is 20 to 40%. In 20% of the fatalities, the cause of death is unrelated to erythroderma.

ALOPECIA

Instructions by the examiner:

- Examine the head. What are your findings? What is the diagnosis?

Presentation of a Case No. 1: (Looking at the Head):

- There is discrete, well-circumscribed patch of hair loss over the scalp in different parts.
- Hair follicles are also seen.
- Eyebrows and eyelashes are present.

My diagnosis is **Alopecia areata**.

Q: What **else** would you like to examine?

A: Hair loss in other parts of the body.

Q: If there is **total loss of body hair**, what it is called?

A: Alopecia universalis.

Presentation of a Case no. 2: (Looking at the Head and Face)

- There is total loss of hair over the whole scalp.
- The eyebrows and lashes are also absent.

My diagnosis is **Alopecia totalis**.

Q: What is **alopecia areata**?

A: It is the localized loss of hair in the scalp. It may be due to autoimmune mechanism. Found in SLE, may be associated with other autoimmune diseases, such as Hashimoto's thyroiditis, Graves disease, pernicious anaemia, diabetes mellitus, vitiligo.

Q: What are the **types** of alopecia?

A: 3 types:

- Alopecia areata (localized loss of hair in the scalp).
- Alopecia totalis (hair loss of entire scalp).
- Alopecia universalis (total loss of body hair).



Alopecia totalis



Alopecia areata



Alopecia in Down's syndrome



Alopecia in linear scleroderma

Q: What are the diagnostic points of alopecia areata?**A:** The following points are diagnostic:

- Usually patches are 1 to 5 cm in diameter.
- Rapid and complete loss of hair, which is patchy in distribution and round or oval in shape.
- At the periphery of bald patches, there are loose hairs that may be broken off leaving short stumps. When they are pulled out, a tapered attenuated bulb is seen as a result of atrophy of that portion, which is called **exclamation point hair**.
- Skin is smooth and shiny without any signs of inflammation and scaling.
- Pruritus is absent.
- In 10% cases, especially in long-standing cases with extensive involvement, nails develop uniform pits that may form transverse or longitudinal lines.

Q: What are the differential diagnoses of alopecia areata?**A:** As follows:

- Non-inflammatory tinea capitis (characterized by multiple scaly lesions and stumps of broken hair and minimal inflammation. Scraping from the scalp reveals hyphae of dermatophyte in microscopical examination in 10% KOH solution).
- Tricho-tillomania (inflammation and scaling are absent, circumscribed lesions are very rare).
- Alopecia of secondary syphilis and SLE (history, clinical features, serological test, scalp biopsy and immunofluorescence will confirm the diagnosis).

Q: What are the causes of alopecia?**A:** It may be Non-scarring and scarring.**Non scarring** (may be diffuse hair loss and focal hair loss):**1. Diffuse hair loss:**

- Abnormality of shedding; telogen effluvium and anagen effluvium.
- Endocrine: Hypopituitarism, hypothyroidism, hyperthyroidism, hypoparathyroidism, androgenetic alopecia, pregnancy.
- Drugs: Cytotoxic drugs, anticoagulants, thyroid antagonists, lithium, oral contraceptives and hypervitaminosis A.
- Others: Severe prolonged illness, malnutrition, deficiency of protein, iron, zinc and biotin, surgery, acute febrile illness and radiotherapy.

2. Focal hair loss: Trichotillomania, traction alopecia, alopecia areata, secondary syphilis and SLE.**Scarring alopecia:**

- Infective: Furuncle, carbuncle, folliculitis, lupus vulgaris, tertiary syphilis, kerion and favus.
- Physical factors: Burn and radiotherapy.
- Chemicals: Acid and alkali.
- Autoimmune: DLE, morphea and cicatricial pemphigoid.
- Neoplastic: Basal cell carcinoma and squamous cell carcinoma.
- Others: Lichen planus, sarcoidosis, lichen sclerosus, follicular mucinosis, pseudopelade, folliculitis decalvans and dissecting cellulitis of scalp.

Q: How to investigate alopecia areata?

A: According to clinical findings:

- Skin scraping for fungus (to exclude tinea capitis).
- ANA, anti-ds DNA (SLE).
- Serological test for syphilis.
- Others: According to suspicion of causes.

Q: How to treat alopecia areata?

A: As follows:

1. Topical:
 - Topical steroid.
 - 1% anthralin cream.
 - Topical minoxidil (2 to 5%).
2. Intralesional injection of steroid (triamcinolone).
3. Photo-chemotherapy using topical or systemic methoxsalen and UVA (PUVA).
4. 308 nm xenon chloride excimer laser has been reported to produce regrowth after 11 to 12 sessions over a period of 9 to 11 weeks.

Q: What is the prognosis?

A: Usually, spontaneous recovery occurs in post-pubertal patients. Predictors of poor prognosis are:

- Presence of atopic dermatitis.
- Childhood onset.
- Widespread involvement.
- Duration longer than 5 years.
- Onychodystrophy.
- Ophiasis (loss may occur confluent along the temporal and occipital scalp).

VITILIGO

Instructions by the examiner:

- Look at here. What are your findings? What is the diagnosis?

Presentation of a Case:

- There are few areas of depigmentation of variable size and shape, surrounded by area of hyperpigmentation.

My diagnosis is **Vitiligo**.

Q: What else do you want to see?

A: I want see vitiligo in other parts of the body (around the eyes, mouth, knee, dorsum of foot, hands, axilla, groin and genitalia). Also, I would like to examine sensation (if lost, suggest tuberculoid leprosy. In advance stage with widespread vitiligo, loss of sensation may occur in lepromatous leprosy).

Q: What is vitiligo? What is the mechanism?

A: It is the area of localized depigmentation, probably due to autoimmune mechanism. Vitiligo is due to focal loss of melanocyte. It affects 1% of population. Generalized vitiligo may occur, usually symmetrical involving hand, wrist, knee, neck, around the eyes, mouth, dorsum of feet. Sites of friction or trauma are often affected. Family history may be present in one-third cases, equally affects both sexes. Although familial in 30% cases, it is not inherited as autosomal dominant or recessive trait, rather seems to have multifactorial genetic basis. Individual is otherwise healthy. Koebner's phenomenon may be present (lesions appear at the site of skin damage).

Q: What diseases are the associated with vitiligo?

A: Vitiligo may be associated with autoimmune diseases, such as systemic sclerosis, Addison's disease, pernicious anaemia, Graves disease, Hashimoto's thyroiditis, premature ovarian failure, diabetes mellitus, primary biliary cirrhosis.



Vitiligo in palms



Vitiligo in hands



Small vitiligo in legs

Q: What are the types of vitiligo?**A:** As follows:

1. Focal vitiligo: Isolated macules or few dermatomal distribution. It has stable course and is unlikely to be associated with thyroid or other vitiligo-associated diseases.
2. Generalized vitiligo: Common, characterized by few to many macules.
3. Acro-facial vitiligo: Involves distal digits and peri-orificial areas.
4. Universal vitiligo: Widespread vitiligo with few remaining normal pigmentation.

Q: What are the differential diagnoses of vitiligo (or, what are the causes of localized hypopigmentation)?**A:** As follows:

- Tinea versicolor: Common in back and chest, it has fine scale. Yeast and hyphal forms are present (detected with 10% KOH solution).
- Pityriasis alba: Associated with fine scale, lesion is poorly defined.
- Tuberculoid leprosy.
- Morphea and lichen sclerosis: Hypopigmented or depigmented area associated with change in skin texture.
- Tuberous sclerosis (ash leaf spot).
- Chemical leucoderma.
- Burn.

Q: What investigations should be done in vitiligo?**A:** Diagnosis is clinical. Investigations are:

1. Woods light examination shows chalky or ivory white fluorescence.
2. Skin scraping for *Malassezia furfur* (to exclude tinea versicolor).
3. Others (according to the suspicion of causes):
4. Blood sugar.
5. Thyroid function tests.
6. Serum cortisol.

Q: How do you treat vitiligo?**A:** As follows:

1. General measures:
 - Reassurance.
 - Use of sunscreen.
 - Use of self-tanning cream containing dihydroxy-acetone.
2. Topical:
 - Steroid (betamethasone and clobetasol propionate).
 - Topical calcipotriene can be added to topical steroid.
 - 0.1% tacrolimus ointment for facial vitiligo.
3. Phototherapy:
 - Narrow band UVB.
 - Topical application of 8-methoxypsoralen followed by UVA.
4. Surgical:
 - Epidermal grafting or autologous minigraft.
 - Transplantation of cultured melanocytes can be applied in patient with segmental vitiligo or with stable vitiligo, which does not respond to other therapy.

N.B. Spontaneous re-pigmentation occurs in 15 to 25% cases.

NEUROFIBROMA

Instructions by the examiner:

- Look at the patient. What is the diagnosis? Or examine this patient.

Presentation of a Case: Case No. 1:

- There are multiple nodular lesions of variable sizes and shapes on the face, both forearms and hands.
- Also, multiple café-au-lait spots on the back of the trunk.

My diagnosis is **Neurofibromatosis type I**.

Q: What else do you like to see?

A: As follows:

- Axillary freckling.
- Lisch nodule (in iris).
- Examination of ear to exclude acoustic neuroma.
- Eyes for optic glioma.
- Spine for scoliosis.
- Blood pressure (high, as it may be associated with pheochromocytoma).



Neurofibroma



Plexiform neurofibroma (arm)



Plexiform neurofibroma (thigh)

Q: What is the **triad** of neurofibromatosis?

A: As follows:

- Neurofibroma.
- Café-au-lait spots.
- Lisch nodules.

Presentation of a Case: Case No. 2:

- There are multiple nodular lesions of variable sizes and shapes on the face, both forearms and hands.
- Also, multiple café-au-lait spots on the back of the trunk.
- There is diffuse overhanging tissues involving arms and thighs with diffuse pigmentation.

My diagnosis is **Plexiform neurofibroma**.

Q: What is neurofibroma?

A: It is a benign tumour of peripheral nerves arising from neurilemmal sheath.

Q: What is neurofibromatosis?

A: It is an autosomal dominant disease characterized by multiple neurofibroma and skin lesions like café-au-lait spots and axillary freckling.

Q: What are the types of neurofibromatosis?

A: 2 types:

- Type 1 or peripheral (also called von Recklinghausen's disease).
- Type 2 or central.

Q: What are the features of type 1 neurofibromatosis?

A: As follows:

- Multiple cutaneous neurofibroma.
- Café-au-lait patches (up to 5 may be found in normal person), 5 mm in pre-pubertal and 15 mm in post-pubertal patients.
- Axillary freckling.
- Hamartoma of iris (Lisch nodules).
- Optic glioma.

Q: What are the features of type 2 neurofibromatosis?

A: As follows:

- Bilateral acoustic neuroma.
- Glioma (cerebral or optic nerve).
- Meningioma.
- Spinal neurofibroma.
- Schwannoma.
- Juvenile posterior subcapsular lenticular opacity.

Q: What are Café-au-lait spots?

A: These are round to ovoid, pale yellow or brown macules, usually present on the trunk. May be 1 cm to more than 15 cm. Up to 5 may be present in a normal person.

Q: What is Lisch nodule?

A: It is a melanocytic hamartoma on the surface of iris, clear to yellow or brown. It increases with age, almost always present in patient older than 20 years. May require slit lamp examination for diagnosis.

Q: What is plexiform neurofibroma?

A: In this type, entire nerve trunk and its branches are involved in diffuse neurofibromatosis with overgrowth of overhanging tissues, leading to gross deformities in temporal and frontal scalp. Commonest site of plexiform neurofibroma are temporal region in relation to trigeminal nerve, upper eyelid and back of the neck. Hyperpigmentation and hypertrichosis of overlying tissue may be found.

Q: What are the **associated findings or complications** of neurofibroma?

A: As follows:

- Kyphoscoliosis.
- Lung cyst (honeycomb lung).
- Pseudoarthrosis and other orthopaedic abnormalities.
- Glioma, meningioma, medulloblastoma.
- Pheochromocytoma (in MEN Ia).
- Posterior mediastinal tumour (called dumb bell tumour).
- Rarely, sarcomatous change (dangerous complication of neurofibromatosis).

Q: Is **biopsy necessary for diagnosis**?

A: No, diagnosis is done clinically.

Q: What is **phacomatosis**?

A: It is a group of diseases in which neurological abnormalities are associated with cutaneous disease.

These are:

- Neurofibromatosis type 1.
- Tuberous sclerosis.
- Von Hippel–Lindau syndrome.
- Sturge–Weber's syndrome.

N.B.: Remember the followings:

- Always check the B.P. Because, it may be associated with pheochromocytoma.
- Acoustic neuroma may be associated with type 2 NF. Patient may have hearing aid (must not miss).
- Axillary or inguinal freckling (called Crowe's sign), present in 2/3rd cases.
- In heart: restrictive cardiomyopathy may be found.
- In lungs: pulmonary fibrosis, pneumothorax may be found.

MYCOSIS FUNGOIDES

Instructions by the examiner:

- Look at the patient's back. Or, perform the general examination.

Presentation of a Case:

- There are multiple, brownish red, indurated plaques of various size and shape over the upper back. The largest one is . . cm in diameter.
- Scratch marks are present.
- Few nodular lesions are noted in the same area.

My diagnosis is **Mycosis fungoides**.



Mycosis fungoides on front



Mycosis fungoides on back



Mycosis fungoides on feet

Q: What **else** do you want to see?

A: I want to see lymph nodes (may be localized or generalized).

Q: What are your **differential diagnoses**?

A: As follows:

- Psoriasis.
- Eczematous dermatitis.
- Contact dermatitis.
- Drug eruption.
- Hansen's disease (leprosy).
- Tinea corporis.

Q: What is **mycosis fungoides**?

A: Mycosis fungoides is rare slowly progressive T cell lymphoma of the skin that develops slowly over many years (sometimes 20 to 30 years), characterized by reddish-brown, scaly and itchy plaques. In early stage, resemble erythematous lesions of psoriasis or eczema.

Q: How does it present? Or what are the clinical features?

A: Initially, it presents with non-specific scaly eruptions, which may be thick and plaque like, confused with eczema or psoriasis. May involve any area of skin. Usually progress very slowly over many years from plaque stage to nodules and finally systemic stage. Extracutaneous involvement (such as liver, lungs, spleen) and lymphadenopathy occur in advance stage only. It is more common in males, 5th to 7th decade.

Q: What are the stages of mycosis fungoides?

A: As follows:

- Stage I: Eczema or psoriasis like lesions.
- Stage II: Plaque like.
- Stage III: Nodules, ulcers, tumours.
- Stage IV: Lymphadenopathy with or without systemic involvement.

Q: What investigation should be done to confirm the diagnosis?

A: Skin biopsy (hallmark is malignant T cell or Sezary–Lautner cells). There may be Pautrier micro-abscess, atypical cells in epidermis, large hyperchromic cells with irregular nuclei called mycosis cell.

Q: What is Sezary syndrome?

A: It is a variant of mycosis fungoides associated with erythroderma characterized by erythroderma, lymphadenopathy and large mononuclear cells (Sezary cells) in the skin and blood.

Prognosis is poor. Extra-corporeal phototherapy (with oral methoxsalen, lymphocyte enriched blood fraction to UVA light and re-infusion of cells into the patient) may be helpful. It is often resistant to treatment and carries poor prognosis.

Q: How to treat mycosis fungoides?

A: As follows:

1. Initially local therapy:
 - Corticosteroid, nitrogen mustard (mechlorethamine), bexarotene gel.
 - PUVA or narrow band UVB phototherapy.
2. After plaque stage: Electron beam radiation.
3. If the disease progresses: PUVA plus retinoid, PUVA plus interferon, bexarotene, α -interferon with or without retinoid, IL-12, denileukin or total skin electron beam may be used.
4. If all fails or in advanced case: Treated for lymphoma such as radiotherapy, chemotherapy (e.g., methotrexate), immunotherapy or electron beam therapy may be used

Q: What is the prognosis?

A: It progresses slowly, usually over decades. Prognosis is better in patient with patch or plaque stage disease and worse in patient with erythroderma, tumour and lymphadenopathy.

TUBEROUS SCLEROSIS

Instructions by the examiner:

- Look at the patient's face or back. Perform the general examination.

Presentation of a Case:

- There are multiple pink or yellowish papules on the face involving cheeks, nasolabial fold, sides of the nose and chin.
- Also few nodules are present on the forehead.

My diagnosis is **Tuberous sclerosis**.

Q: What are name of the **papules** on the face?

A: These are angiofibroma called adenoma sebaceum.

Q: What **else** do you like to see? Or what are the **skin lesions**?

A: As follows:

- Subungual fibroma (nodule arising from the nail bed).
- Shagreen patches (firm, flesh coloured, patches of leathery thick skin over the lower back).
- Ash leaf patches (hypopigmented areas of skin).
- Café-au-lait spots present in 30% cases.



Adenoma sebaceum in tuberous sclerosis



Shagreen patch of the same patient



Ash leaf patch in tuberous sclerosis



Subungual fibroma

Q: What **history** do you like to take?

A: As follows:

- Family history of similar disease.
- History of convulsion and mental retardation.

Q: What is **tuberous sclerosis**?

A: It is an autosomal dominant disease characterized by triad of mental retardation (or learning disability), epilepsy and skin lesions.

Q: What other lesions may be associated?**A:** As follows:

- CNS hamartomas: Cortical tubers and subependymal hamartomas, cerebral glioma and calcification of basal ganglia.
- Retinal phacoma (glial mass).
- Hyperplastic gum.
- Benign rhabdomyoma of heart.
- Renal angiomyolipoma.
- Cysts in lung, liver, pancreas, kidneys and bones.

Q: What investigations should be done?**A:** As follows:

- skull x-ray shows tram-line calcification at the basal ganglia.
- CT scan or MRI of brain

Q: How to treat?**A:** No specific treatment.

- Symptomatic treatment for seizure.
- Genetic counselling should be done.

Q: What is the cause of death?**A:** Usually from seizure, intercurrent illness or associated neoplasm.

KAPOSI'S SARCOMA

Instructions by the examiner:

- Look at the patient's back. Or, perform the general examination.

Presentation of a Case:

- There are multiple red or purple or brownish plaques and nodules of various sizes and shapes all over the back.

My differential diagnoses are:

- Drug rash.
- Haemangioma.
- Bacillary angiomatosis.
- Cutaneous tuberculosis.
- Sarcoidosis.
- Cutaneous lymphoma.
- Kaposi sarcoma.

Q: What is Kaposi sarcoma?

A: It is a tumour of vascular and lymphatic endothelium characterized by multiple purplish nodules and plaque caused by human herpes virus 8 (HHV8). It is an AIDS defining illness.

Q: What is the cause?

A: Human herpes virus 8 (HHV8), also known as Kaposi's sarcoma associated herpes virus (KSHV). 70 to 100% of Kaposi's sarcoma have antibody to HHV8 compared with 1 to 5% in general population.

Q: What are the types?

A: 4 types:

- Classic or sporadic form: Affects middle aged male, common in Jews and Mediterranean region, indolent course, mainly affects lower limbs, confined to skin and is not fatal.
- African endemic KS: Occurs in children and younger men, more aggressive and ultimately fatal. There is violaceous skin plaque, may be associated with generalized lymphadenopathy in children.
- Transplantation associated KS (or KS in iatrogenically immunocompromised patients), especially in patients getting immunosuppressive therapy. It often regresses when the therapy is stopped.
- AIDS-related KS: More aggressive, often rapidly progress to plaques and nodules affecting upper trunk, face and oral mucosa. Affects 1/3rd patients with AIDS, common in homosexuals. About 1/3rd develop a second malignancy like lymphoma, leukaemia, myeloma etc. In AIDS patient, it may occur with high CD4 count and low viral load.



Kaposi sarcoma

Q: What are the presentations or clinical features?

A: As follows:

- In early case: Small, raised, non-pruritic, reddish purple nodule on the skin or discoloration of oral mucosa or swollen lymph node. Commonly affects lower limbs, back, face, mouth and genitalia. Cutaneous lesions may be solitary, localized or disseminated.
- With progression, the skin lesions become larger and numerous. The lesions may be macular, patch, plaque, nodular and exophytic.
- Chronic leg oedema may occur.
- Visceral disease occurs in 10% at presentation. Commonly involved sites are lymph nodes, oral cavity, GIT, lungs, heart, CNS etc.

Q: How to diagnose?

A: By biopsy of suspicious lesion. If needed, internal imaging may be done.

Q: How to treat?

A: Depends on the subtype, localized or associated with systemic disease:

- Localized mucocutaneous disease responds to cryotherapy, radiotherapy, surgical excision, intralesional vinblastine, topical immunotherapy (imiquimod), interferon- α .
- AIDS-related KS: Patient should first get HAART, which improves Kaposi sarcoma.
- More widespread disease or disease affecting internal organs, is treated with systemic therapy with interferon- α , liposomal anthracyclines or paclitaxel. IV chemotherapy (e.g., combination of vincristine and bleomycin or newer liposomal preparation of doxorubicin) and immunotherapy may be given.
- In KS from immunosuppression: Immunosuppressive therapy should be reduced or discontinued.

PITYRIASIS VERSICOLOR (TINEA VERSICOLOR)

Instructions by the examiner:

- Look at the patient's chest. Or, perform the general examination.

Presentation of a case:

- There are multiple hypopigmented macules of variable size and shape involving the front of the chest, both sides of neck and upper part of back.

My diagnosis is **Pityriasis (tinea) versicolor**.

Q: What are the **differential diagnoses**?

A: As follows:

- Vitiligo.
- Other fungal infections like tinea corporis.

Q: What are the **sites of lesion** of pityriasis versicolor?

A: Trunk, upper arm, neck, groin.



Pityriasis versicolor
in neck



Pityriasis versicolor
in face



Pityriasis versicolor
in chest



Pityriasis versicolor
in back

Q: What is **pityriasis versicolor**? What is the **cause**? What are the **clinical features**?

A: It is a benign superficial skin infection caused by fungus called *Malassezia furfur*. Common in warm temperature, more severe in immunocompromised. Clinical Features:

- Upper trunk is mostly involved. Lesions are small white spots on the trunk, neck, upper arm, face.
- May be velvety, faintly brown macules.
- May fuse together forming bigger area of depigmentation.
- On scratching, fine scales may be separated from the patch.
- No itching.

Q: How to **confirm** your diagnosis?

A: Diagnosis is clinical.

- Skin scrapping for fungus: Direct microscopic examination of scales (stain with potassium hydroxide), which shows large blunt hyphae and thick walled budding spore (spaghetti and meat balls).
- Wood's Lamp shows blue-green fluorescence of scales.

Q: How to treat?**A:** As follows:

1. Topical treatment:
 - Selenium sulphide (2.5%) lotion may be applied from neck to waist for 5 to 15 minutes continued for 7 days. Repeated weekly for a month and then monthly for maintenance.
 - Ketoconazole shampoo (1% or 2%): Applied and left for 5 minutes, may be used weekly.
 - Azole creams (ketoconazole, econazole, miconazole, clotrimazole).
 - Terbinafine 1% solution.
 - General measures—personal hygiene should be maintained, inner garments should be boiled and changed daily.
2. Oral antifungal:
 - Ketoconazole 200 mg daily for 1 week or 400 mg in a single dose, may be repeated at monthly intervals.
 - Fluconazole 300 mg 2 doses 14 days apart Or 400 mg once may be effective, can be repeated at monthly
 - Itraconazole may be given, 200 mg once daily for 7 days.

N.B. Recurrence is quite common. Maintenance treatment may be necessary.

MISCELLANEOUS 12

FACE IN DIFFERENT DISEASES	965	STURGE–WEBER’S SYNDROME	980
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'Experience is never limited, and it is never complete'
—Henry James

FACE IN DIFFERENT DISEASES

Instructions by the examiner:

- Look at the face. Or, examine the face. What is your diagnosis? What relevants do you like to see?

There is likely to be obvious diagnosis by looking at the face. Further examination depends on the suspicion of the underlying cause. Possible diagnoses are as follows:

- Myxoedematous face (pages 510, 521).
- Thyrotoxic face or Graves' disease (pages 512 and 531).
- Cushingoid face (page 555).
- Acromegalic face (page 548).
- Mongoloid face (Down syndrome; pages 486, 974).
- Haemolytic face (frontal and parietal bossing and prominent malar bones, page 486).
- Puffy face (page 966).
- Leonine facies (lepromatous leprosy, page 57).
- Facial palsy (page 726).
- Parkinsonian face (page 685).
- Marfanoid face (page 201).
- Mitral face (page 140).
- Myopathic face (pages 707, 873).
- Nephrotic face (page 601).
- Achondroplasia (skull appears enlarged, page 574).
- Superior vena caval (SVC) obstruction (page 61).
- Sturge–Weber's syndrome (page 980).
- Hepatic facies (muddy or pigmented discolouration, pinched face and sunken eyes).
- Hippocratic facies (in advance peritonitis): sunken eyes, collapsed temples, pinched nose, crust on lips, clammy forehead.
- Psychiatric disorders (depressed or anxious facies).
- Butterfly rash (page 969).
- Systemic sclerosis (page 757).
- Myasthenic face (page 873).

- Turner's face (page 971).
- Virile (virilization in female).
- Tabetic face.
- Paget's disease.
- Facial asymmetry (hemiplegia and hemiatrophy).
- Lupus pernio in sarcoidosis.

Q: What are the causes of depressed nasal bridge?

A: As follows:

- Trauma.
- Tuberculosis (lupus vulgaris).
- Leprosy.
- Sarcoidosis.
- Congenital syphilis (also tertiary).
- Wegener's granulomatosis.
- Fungal infection (deep).
- Idiopathic midline granuloma.
- Cutaneous leishmaniasis.



Lupus pernio in sarcoidosis



Depressed nasal bridge in Wegener's granulomatosis



Puffy face in nephrotic syndrome



Malar flush

Q: What are the causes of puffy face?

A: As follows:

- Nephrotic syndrome.
- Acute glomerulonephritis.
- Myxoedema.
- SVC obstruction.
- Acromegaly.
- Angioneurotic oedema.
- Cushingoid face.
- Chronic alcoholism.
- Severe congestive cardiac failure.
- Hereditary angioedema.

Q: What are the causes of malar flush?**A:** As follows:

- Normal person.
- Mitral stenosis.
- Hypothyroidism.
- Polycythaemia.

Q: What are the causes of plethoric face?**A:** As follows:

- Normal physiological.
- Polycythaemia (due to any cause).
- Cushing's syndrome.
- Alcoholism.
- SVC obstruction.



Plethoric face in polycythaemia



Plethoric face in Cushing syndrome



Chloasma/melasma

Q: What are the causes of chloasma or melasma?**A:** It is a discrete pigmentation in the face of females, due to imbalance between oestrogen and progesterone. Melanocyte-stimulating hormone (MSH) is normal. The causes are:

- Physiological: pregnancy.
- Sunlight exposure.
- Drugs (oral contraceptive and phenytoin).
- Ovarian tumour (rare).

WEGENER'S GRANULOMATOSIS

Def: It is a disorder of unknown aetiology characterized by necrotizing granulomatous vasculitis of upper and lower respiratory tract with Glomerulonephritis (focal, segmental, necrotizing). It is also called granulomatous polyangiitis.



Wegener's granulomatosis (nose)



Wegener's granulomatosis (eye)

Clinical features:

- Nasal discharge, epistaxis, nasal obstruction, nasal crust, rhinitis and sinusitis. If untreated, destruction of nasal bone and cartilage causes depressed nose.
- Deafness (due to serous otitis media).
- Respiratory problems: cough, haemoptysis, chest pain, breathlessness.
- Eye: proptosis, conjunctivitis, episcleritis, iritis.
- Features of glomerulonephritis or renal failure.

Investigations:

- CBC with ESR (shows leucocytosis with very high ESR).
- CRP (high).
- Urine RME (shows proteinuria).
- S. creatinine, blood urea.
- Chest x-ray: single or multiple nodules (migrating lung lesion in 50% cases).
- MRI of chest.
- Biopsy: from nasal lesions or nasal crusts and also from kidney (shows necrotizing vasculitis with granuloma formation).
- Serum c-ANCA level: high (also done to see improvement and relapse).

Q: How to treat?

A: As follows:

- Cyclophosphamide (2 mg/kg) **plus** prednisolone (1 mg/kg), OR
- IV cyclophosphamide (15 mg/kg) **plus** IV methylprednisolone (10 mg/kg) every fortnight and then every month.
- Once remission occurs (takes 3 to 6 months), low dose prednisolone with azathioprine, or MTX or mycophenolate mofetil may be given.
- Rituximab with high dose prednisolone is equally effective as oral cyclophosphamide.
- Oral co-trimoxazole (960 mg, three times weekly) is given to prevent pneumocystis pneumonia.
- To check relapse, periodic measurement of c-ANCA is performed.

BUTTERFLY RASH

Instructions by the examiner:

- Look at the face. Or, examine the face.

Look carefully to the following points:

- Rash distribution (check whether present in other parts of face) and character, scaly desquamation and redness or other colour, follicular plugging.
- Any nodular lesion (in face or ear lobule).
- Heliotrope rash (eyelid), telangiectasia, tightening or thickening of skin and pinched up nose.
- Alopecia.
- Mouth ulcer.

Presentation of a Case:

- There are multiple skin rashes on the face along the butterfly distribution, also involving the forehead and cheeks (mention, if any). Some are scaly and reddish with clear margin, more marked on the right (or left) side of face.
- There is presence of nodule or telangiectasia, vitiligo and hyper- and hypopigmentation.

Q: What are the differential diagnoses for butterfly rash?

A: As follows:

- SLE or discoid lupus erythematosus (DLE).
- Dermatomyositis.
- Mixed connective tissue disease (MCTD).
- Sarcoidosis.
- Drug rash.
- Acne rosacea (characterized by red patch with telangiectasia on the face with papules and pustules, which are absent in SLE).
- Lepromatous leprosy.
- Post kala-azar dermal leishmaniasis (PKDL).



Butterfly rash (SLE)



Butterfly rash
(dermatomyositis)



Skin rash in leg
and foot (SLE)



Mouth ulcer in SLE

Q: What **else** do you want to examine?

A: As follows:

- Rash in other parts of the body, alopecia and mouth ulcer SLE.
- Proximal myopathy (dermatomyositis).
- Sensation over skin lesion (leprosy).
- History of PKDL.
- History of drugs.
- Check for any lymphadenopathy, hepatomegaly, splenomegaly and erythema nodosum (sarcoidosis).

TURNER'S SYNDROME

Instructions by the examiner:

- Look at the patient. What is your diagnosis?

Proceed and Present as Follows: (Ask the Patient her Age. The Patient is a Female with Obvious Short Stature for her Age).

- Short and webbed neck, low hairline and redundant skinfold on the back of neck.
- Face: small lower jaw (micrognathia), small and fish like mouth, high arched palate and low set and deformed ears.
- Chest: broad, wide apart nipples (shield like chest).
- Hand: short fourth metacarpal (other metacarpals may be short), lymphoedema of hands (also feet), hypoplastic nails.
- Elbow: increased carrying angles (cubitus valgus).

My diagnosis is **Turner's syndrome**.

Q: Why does **webbing** of the neck occur?

A: It occurs due to the fan like fold of skin extending from shoulder to neck or an abnormal splaying, out of trapezius muscle.

Q: What are the **causes** of webbing of the neck?

A: As follows:

- Turner's syndrome.
- Noonan's syndrome.
- Watson's syndrome.
- Klippel–Feil syndrome.
- Diamond–Blackfan anaemia.



Webbing of neck



Low hairline



Short fourth metacarpal



Shield-like chest

Q: What is **Turner's syndrome**?

A: It is a sex chromosomal abnormality, characterized by absence of one of X chromosomes (45, XO). It only affects females. All or part of one X chromosome is deleted, leading to failure of ovary development. Externally, patient appears female, but does not produce female sex hormones. Hence, the patient remains sexually immature.

Q: What are the clinical features?

A: Usually presents with amenorrhoea, underdeveloped secondary sexual characters. Features are:

- Short stature.
- Short, webbed neck, low hairline, redundant skin fold on the back of neck.
- Face: small lower jaw (micrognathia), small, fish-like mouth, high arched palate, low-set deformed ears.
- Chest: broad, wide apart nipples (shield-like chest).
- Hand: short fourth metacarpal (other metacarpals may be short), lymphoedema of hands (also feet) and hypoplastic nails.
- Elbow: increased carrying angles (cubitus valgus).

Q: What investigations do you suggest?

A: As follows:

- Karyotyping from buccal smear: 45 (XO) is classical, occasionally 46 (XX) mosaics.
- Ultrasonogram (small uterus, fallopian tube and streak gonad).
- Hormone assay (low oestrogen, high luteinizing hormone and follicle-stimulating hormone).

Q: What is mosaicism?

A: The presence of two or more cell lines within the body, either a 46XX or 46XY karyotype.

Q: How to treat Turner's syndrome?

A: As follows:

- Oestrogen therapy at puberty.
- Growth hormone may accelerate height, but it is not yet established whether there is any effect on final height.
- Gonadal tumour may occur rarely, especially in mosaic involving Y chromosome. Hence, it should be removed.

Q: What are the associations or diseases that occur in Turner's syndrome?

A: As follows:

1. Heart:
 - Coarctation of aorta (10–20% cases). There may be atrial septal defect (ASD), ventricular septal defect (VSD) and aortic stenosis (AS).
 - Hypertension.
2. Kidney:
 - Horseshoe kidney.
 - Hydronephrosis.
3. Others (incidence is more):
 - Diabetes mellitus (DM).
 - Hashimoto thyroiditis (may be frank hypothyroidism in 20% cases).
 - Lymphoedema in infancy.
 - Red and green colour blindness.
 - Strabismus and ptosis.
 - Premature osteoporosis.
 - Pigmented nevi.
 - Mental retardation (rare).

Noonan's syndrome

It is also called male Turner. Noonan's syndrome is characterized by:

- Short stature.
- Mental retardation (common).
- Downward slanting and wide spaced eyes.
- Low set ear.
- Webbing of the neck.
- Low posterior hairline.
- Pulmonary stenosis.

It may affect both male and female equally. Female patients have Turner phenotype but with normal 46, XX. They have normal ovarian function and normal fertility. In male, there is 46XY.

Cardiac lesion is present more on right side, usually pulmonary stenosis. In Turner's syndrome, left sided cardiac lesion is more.

DOWN'S SYNDROME

Instructions by the examiner:

- Examine the patient. What are your findings? What else do you want to examine?

Proceed and Present as Follows:

1. Face:
 - Appears flat.
 - Nasal bridge appears flat.
 - Low set, small ears.
 - Mouth appears small and tends to remain open with high arched palate.
 - Tongue appears protruding with large, horizontal fissure.
2. Eyes:
 - Epicanthic folds and slanting eyes.
 - Brush-field spots on iris (yellow speckles).
 - Conjunctivitis.
3. Neck: short and wide.
4. Hands: single palmar crease (simian) and short stubby finger. Hand looks small and round (short, broad hands) and has clinodactyly (short inward curving of little finger).
5. Short stature, hypotonia, joint hyperextensibility.
6. Heart disease (VSD is common, also ASD, PDA, tetralogy of Fallot and mitral regurgitation due to endocardial cushion defect).
7. Straight pubic hair, gap between first and second toes.
8. Low IQ (from mild to severe).

N.B. The child is fond of music.

Q: What **history** do you like to take?

A: Maternal age during pregnancy (incidence is high with advancing maternal age).

Q: What are the **complications** of Down's syndrome?

A: As follows:

- Mental retardation (mild to severe). There is learning disability or cognitive impairment.
- Haematological: In neonates, acute myeloid leukaemia and in older children, acute lymphoid leukaemia.
- GIT: Duodenal atresia, Hirschsprung disease, Meckel's diverticulum, imperforate anus.
- Presenile dementia of Alzheimer's type (in third to fourth decade).
- Endocrine: Autoimmune hypothyroidism, diabetes mellitus type I.
- Infertility almost in all males, female may be fertile.
- Lenticular opacity.



Down's syndrome

Horizontal fissure
in tongueSingle palmar crease
in Down's syndromeLymphoedema hand
in Down's syndromeLymphoedema foot in
Down's syndrome and
gap between first and
second toe**Q: What is Down's syndrome?**

A: It is a chromosomal abnormality, trisomy 21 (47, XX/XY, + 21), caused by presence of all or part of an extra 21 chromosome.

Q: What are the types?

A: 3 types:

- Trisomy 21 (47, XX/XY, + 21), commonest, 95%.
- Mosaic variant, 1%.
- Translocation variant, 4%.

Q: How to diagnose Down's syndrome?

A: By karyotyping.

Q: How prenatal screening is done?

A: As follows:

1. First trimester:
 - Ultrasonography to see nuchal translucency.
 - Serum human chorionic gonadotropin (β hCG).
 - Pregnancy-associated plasma protein A (PAPP-A).
2. 13 to 20 weeks:
 - Maternal serum for α -foetoprotein, hCG and unconjugated oestriol (uE_3).
 - Foetal USG.
 - Amniocentesis.

N.B. Mother with risk of Down's syndrome: Chorionic villous sampling before 13 weeks of gestation or amniocentesis after 15 weeks of pregnancy may be done.

BILATERAL PAROTID ENLARGEMENT

Instructions by the examiner:

- Look at the face of the patient. What is your diagnosis?

Presentation of a Case:

- There is bilateral swelling of parotid glands, which are firm and nontender.

My diagnosis is **Bilateral parotid enlargement**.



Bilateral parotid enlargement



Bilateral parotid enlargement

Q: What are the **causes** of bilateral parotid enlargement?

A: As follows:

- Sarcoidosis.
- Alcoholic liver disease or chronic alcoholism.
- Bilateral mumps (usually it is painful).
- Sjögren's syndrome.
- Malnutrition.
- DM.
- Lymphoma.
- Leukaemia.
- Mikulicz syndrome.

Q: What **else** do you want to examine in this patient?

A: As follows:

- Dryness of eye and mouth (Sjögren's syndrome).
- Lymph node (sarcoidosis, lymphoma, leukaemia).
- Other evidences of sarcoidosis (erythema nodosum, lupus pernio).
- Other collagen diseases (in secondary Sjögren's syndrome).

Q: What is Mikulicz syndrome?

A: It is the enlargement of salivary and lachrymal glands. The causes are:

- Sarcoidosis.
- Lymphoma.
- Leukaemia.
- Tuberculosis.
- Sjögren's syndrome.

*N.B.: Secondary Sjögren's syndrome is called **Mikulicz disease** (where no salivary or lachrymal gland enlargement is present).*

XANTHELASMA

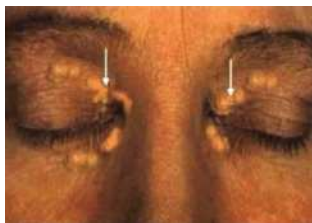
Instructions by the examiner:

- Examine the face. What does it present?

Presentation of a Case:

- There are yellowish plaque or nodular lesions at the upper eyelid (may be also in lower eyelid), near the inner canthus in one or both eyes.

My diagnosis is **Xanthelasma**.



Xanthelasma



Corneal arcus



Tuberous xanthoma (elbow)



Tendon xanthoma in Achilles tendon



Tendon xanthoma (feet)



Lipaemia retinalis



Tendon xanthoma (knuckle)



Eruptive xanthoma

Q: What is **xanthelasma**? What are the **causes** of xanthelasma?

A: These are yellowish plaque in the subcutaneous or intracutaneous tissues due to deposition of cholesterol or lipids in the eyelids. The causes are:

1. Familial.
2. Primary biliary cirrhosis.
3. Hyperlipidaemia (types II and III).
4. Others
 - Hypothyroidism.
 - Diabetes mellitus.
 - Nephrotic syndrome.
 - Alcoholism.
 - Drugs (thiazide diuretic, cyclosporine, steroid, androgen and oral contraceptive pill).

Q: What **else** do you want to examine?

A: Corneal arcus, xanthoma in other parts (patella, Achilles tendon and dorsum of the hand) and evidence of primary disease.

Q: What is **xanthoma**? What are the various **types** of xanthoma?

A: Xanthomas are deposits of fatty material in the skin and subcutaneous tissue and tendons due to primary or secondary hyperlipidaemia. 4 types:

- Eruptive xanthoma (multiple, yellow or papule in trunk and buttock).
- Tendon xanthoma (subcutaneous nodules attached to tendons over dorsum of fingers and Achilles tendon).
- Tuberous xanthoma (elbow and knee).
- Palmar xanthoma.

Q: What **diseases are associated** with hypercholesterolaemia and hypertriglyceridaemia?

A: As follows:

- Hypercholesterolaemia: Tendon xanthoma, tuberous xanthoma, xanthelasma, corneal arcus, atherosclerosis and IHD.
- Hypertriglyceridaemia: Acute pancreatitis, lipaemia retinalis, retinal vein thrombosis (alone it is not associated with atherosclerosis and IHD).
- Hypertriglyceridaemia associated with eruptive xanthoma.
- Mixed hyperlipidaemia: Tuberous, tendon and palmar xanthoma.

Q: What are the **causes of lipaemia retinalis**?

A: Hypertriglyceridaemia and DM.

Q: How to **treat** hypercholesterolaemia?

A: As follows:

1. General measures:
 - Weight reduction in obesity, exercise, diet (avoid cholesterol-containing diet and animal fat).
 - Avoid smoking and alcohol.
 - Treatment of primary disease.
2. Lipid lowering drugs may be given.
 - HMG Co-A reductase inhibitors (simvastatin, pravastatin and lovastatin) are used in treating hypercholesterolaemia.
 - Fibrates (fenofibrate, gemfibrozil) are used in treating hypertriglyceridaemia.
 - Others: nicotinic acid, probucol and fish oil (omega-3 triglyceride).

N.B. Tendon xanthoma may be confused with:

- *Rheumatoid nodule.*
- *Tophi of gout.*
- *Neurofibroma.*
- *Lipoma.*

STURGE–WEBER'S SYNDROME

Instructions by the examiner:

- Examine the face. What are your findings? What is the diagnosis?

Presentation of a Case:

- There is port-wine stain (reddish, slightly pigmented area) at the right outer part of face near the outer and upper part of right eye.

My diagnosis is **Sturge–Weber's syndrome**.

Q: What **history** do you like to take into consideration?

A: Epilepsy (on the side opposite to the skin lesion).

Q: What is **Sturge–Weber's syndrome**?

A: It is a disease characterized by capillary or cavernous haemangioma (port-wine stain) along the cutaneous division of trigeminal nerve (commonly first or second division). There is venous haemangioma in subjacent leptomeninges, which may spread causing atrophy of cortex. It may be sporadic or inherited as autosomal dominant. Underlying brain damage is a rare cause of infantile hemiplegia, mental retardation and epilepsy. Lesion is on the face or the trunk in a dermatological distribution. In middle age, it may be dark with formation of angiomatous nodules. The patient may have mental retardation.

Q: What **investigations** do you suggest?

A: As follows:

- X-ray of the skull that shows **tramline** calcification (in cortical capillaries).
- Computed tomography (CT) or magnetic resonance imaging (MRI) investigations.

Q: What are the **findings in the eye** in Sturge–Weber's syndrome?

A: As follows:

- Glaucoma (which may lead to blindness).
- Strabismus.
- Buphthalmos (ox-eye appearance).
- Optic atrophy.
- Angiomata of choroid.



Sturge–Weber's syndrome

Q: What are the **neurological findings**?

A: Jacksonian epilepsy, contralateral hemianopia, hemisensory disturbance, hemiparesis, hemianopia, low IQ.

Treatment: Unsatisfactory. Only symptomatic treatment.

- Laser therapy for skin lesion.
- Control of convulsion.
- Ophthalmologist opinion for glaucoma, choroidal angioma.

HEREDITARY HAEMORRHAGIC TELANGIECTASIA

Instructions by the examiner:

- Examine the face. What are your findings? What is the diagnosis?

Presentation of a Case:

- There is telangiectasia in lip, face, under surface of tongue, palate, buccal mucosa and nasal mucosa.

My diagnosis is **Hereditary haemorrhagic telangiectasia** (also called Osler–Weber–Rendu syndrome).

Q: What is telangiectasia?

A: It is the localized collection of multiple non-contractile capillaries. If punctured, it shows prolonged bleeding time.

Q: What are the sites of telangiectasia?

A: It is found in lip, face, tongue (also under surface), buccal mucosa, nasal mucosa, nail bed, palm, feet and gastrointestinal tract, also, in any part of the body (lungs, nervous system, liver etc.).



Telangiectasia
(palate)



Telangiectasia
(tongue)



Telangiectasia
(toe and sole)



Telangiectasia (lip)

Q: What are the causes of telangiectasia?

A: As follows:

- SLE.
- Dermatomyositis.
- Necrobiosis lipoidica diabetorum.
- Systemic sclerosis.
- Carcinoid syndrome.
- Topical steroid.
- Ataxia telangiectasia.
- Hereditary haemorrhagic telangiectasia.

Q: What is hereditary haemorrhagic telangiectasia?

A: It is a disease inherited as autosomal dominant, characterized by the formation of multiple telangiectasia in the skin and mucous membrane in different parts of the body. It is a family disorder, caused by mutations in various genes.

Q: What are the presentations?**A:** As follows:

- Epistaxis (common), usually recurrent and sometimes, the only site of bleeding.
- GIT bleeding.
- Haemoptysis.
- Bleeding from other sites.
- Anaemia (due to chronic blood loss, especially from GIT).
- Sometimes, pulmonary arteriovenous fistula may develop resulting in haemoptysis, cyanosis and clubbing.
- Paradoxical embolism, stroke and cerebral abscess may occur.
- AV aneurysm may also occur in liver.
- In the eye, bloody tear (conjunctival telangiectasia), retinal haemorrhage and even detachment may occur.
- Neurological telangiectasia may cause haemorrhage and the formation of bland or mycotic aneurysm.

Q: How to treat HHT?**A:** As follows:

1. General measures:
 - Continuous iron therapy.
 - Sometimes, blood transfusion in severe cases.
2. If epistaxis is the main symptom:
 - Oestrogen therapy (induces squamous metaplasia of nasal mucosa).
 - Laser ablation.
 - Septal dermoplasty.
 - Antifibrinolytic agent (aminocaproic acid).
3. Skin lesion:
 - Cosmetic surgery
 - Laser ablation.
4. GIT: Photocoagulation therapy.
5. Lung arteriovenous malformation: embolization or ligation of artery or surgical resection.
6. Individual lesions should not be cauterized.

YELLOW NAIL SYNDROME

Instructions by the examiner:

- Examine the fingers or toes. What are your findings? What is the diagnosis? Perform the general examination.

Presentation of a Case:

- The nails are thick, curved from side to side and yellow (or greenish yellow) with onycholysis (separation of distal part of nail plate from its bed).
- Cuticles and lunulae are lost. Finger tips are bulbous and uncovered (stunted nail growth).

My diagnosis is **Yellow nail syndrome**.

Q: What else do you like to examine?

A: Ankle oedema (non-pitting). Also, I want to examine the chest to check for bronchiectasis and pleural effusion (also may be COPD and malignant neoplasm).



Yellow nail (fingers)



Yellow nail (toes)



Yellow nail syndrome (lymphoedema)

Q: What is yellow nail syndrome?

A: It is an inherited disease associated with hypoplasia of the lymphatic system, characterized by thick and yellow nails and lymphoedema of legs.

Q: What are the associations?

A: As follows:

- Thyroid disease (hypothyroidism, Hashimoto's thyroiditis, thyrotoxicosis).
- Malignancy (melanoma, carcinoma of lung, breast, Hodgkin's disease).
- Hypogammaglobulinaemia.
- Rheumatoid arthritis.

Q: How to treat?

A: No specific treatment. Only symptomatic and supportive treatment.

SKIN CANCERS

Common skin cancers are squamous cell carcinoma, basal cell carcinoma, malignant melanoma and mycosis fungoides.

SQUAMOUS CELL CARCINOMA (SCC)

It is the second common skin cancer, arises from epidermal keratinocytes, more in elderly males and smokers. Common sites are chronically sun-exposed areas such as scalp, ears, face and dorsum of hands.

It develops as a painful keratotic nodule in a pre-existing area of dysplasia or newly developed erythematous, infiltrated, warty nodule or plaque which may ulcerate. It may be well-differentiated or poorly differentiated which may be infiltrative and may ulcerate. SCC of lips and ears are more likely to metastasise to draining lymph nodes, especially in immunosuppressed patients.

Definitive diagnosis by skin biopsy. Treatment of choice is early diagnosis and complete surgical excision. Other options are curettage and cautery for small, low risk lesions and radiotherapy, if surgery is not possible.



Squamous cell carcinoma



Basal cell carcinoma



Malignant melanoma
(face)



Malignant melanoma
(back)

BASAL CELL CARCINOMA (BCC)

BCC is a slowly growing tumour, commonly occurs at sites of moderate sun exposure, particularly the face, head and neck area, common in male, rarely metastasize. Lesions may ulcerate and invade locally, so it is called 'rodent ulcer'.

Basal cell carcinoma (BCC) arises from immature pluripotent epidermal cells. Mutations in PTCH-1 tumour suppressor gene may have a role in its pathogenesis.

Treatment of choice is wide excision with histology to ensure clear and adequate tumour margins. Superficial BCC can be managed with non-surgical treatment, including cryotherapy, photodynamic therapy and topical imiquimod. Radiotherapy may be given if surgery is not possible. Vismodegib is a new oral therapy for advanced or inoperable BCC.

MALIGNANT MELANOMA

It is the most serious form of skin cancer because early metastasis can occur. Melanoma is common in later life but can occur at any age, any site and in either sex, but typically affects the leg in females and back in males, rare before puberty. About 50% of melanomas arise from a pre-existing naevus.

Most likely cause is excessive exposure to sunlight, especially intermittent intense exposure and sunburn in childhood. Most melanomas are sporadic and risk factors are fair skin, multiple melanocytic naevi (>50), sun sensitivity, freckles, red hair, immunosuppression, atypical mole syndrome, giant congenital melanocytic naevi, lentigo maligna and family history of malignant melanoma.

Surgery is the only curative treatment, wide excision with a 1 cm margin for thin melanomas (<1 mm) or 3 cm margin for thicker melanomas (>2 mm). Treatment for metastatic disease are removal of regional lymph nodes, isolated limb perfusion, radiotherapy, immunotherapy and chemotherapy. Newer therapies are mitogen activated protein (MAP) kinase inhibitor, BRAF inhibitors (vemurafenib), MEK inhibitors (trametinib), CTLA4 antibody (ipilimumab) and programmed death 1 protein antibody (PD-1 antibody, pembrolizumab, nivolumab). Combination of ipilimumab and nivolumab have shown good results with minimum toxicity.

NORMAL CASE

It is not uncommon that occasionally examiner may ask to examine a normal patient to assess the efficiency of a candidate's clinical skill or to see whether a candidate can examine systematically and properly.

- It is frequently asked: 'Examine the fundus of this patient'. The candidate makes many **commissions** in a normal fundus.
- Examine the abdomen: There may not be any abnormality and candidate should present the case sincerely that there are no abnormal findings. However, remember that if the examiner asks to examine the abdomen again, probably some findings have been missed (just palpable liver, just palpable spleen and small abdominal mass). This time, examine very carefully.
- Examine the cardiovascular system. There may not be any abnormality in the heart and the candidate make a 'commission' of having murmur or rub or valvular lesion or abnormal heart sound.
- Perform the neurological examination. Examine the reflexes, sensory test, cranial nerve etc.
- Show how to see anaemia, jaundice, clubbing, oedema, lymph nodes, thyroid, pulse (quite common in undergraduate examination).

N.B. Remember the following points:

- *Commission is dangerous than omission.*
- *Omission is safer than commission.*

*'Now, this is not the end. It is not even the beginning of the end.
But it is perhaps, the end of the beginning'.
—Winston Churchill*

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DATA INTERPRETATION

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'A good clinician is a good physician. Clinical medicine will always persist as a basic diagnostic tool. Investigations, even sophisticated ones, will remain as complementary to the clinician'.

—The author

HEPATOLOGY

Case 01: Obstructive Jaundice

A 45-year-old man presented with the following blood report:

- Serum bilirubin: 20 mg/dL (normal up to 1.2 mg/dL).
- Serum glutamic pyruvate transaminase (SGPT): 80 U/L (normal <20 U/L).
- Serum alkaline phosphatase: 1400 U/L (normal 20–100 U/L).
- Prothrombin time: 24 seconds (control: 12 seconds).

Q: What is the likely **diagnosis**?

A: Obstructive jaundice.

Q: Mention **three** important points in the **history** of the patient.

A: As follows:

- Generalized itching.
- Stool: Clay, pale or muddy-coloured.
- Pain in the epigastrium or upper abdomen.

Q: Mention **one** **investigation** helpful for the diagnosis.

A: Ultrasonography (USG) of the whole abdomen (or hepatobiliary system).

Q: Write down **four** important **causes** of this condition.

A: As follows:

- Choledocholithiasis.
- Carcinoma of the head of pancreas.
- Periapillary carcinoma.
- Cholangiocarcinoma.

N.B. High bilirubin with high alkaline phosphatase is highly suggestive of obstructive jaundice. SGPT may be slightly high. Other investigations such as computed tomographic (CT) scan of the abdomen, endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP) may be necessary.

Case 02: Acute Viral Hepatitis

A 26-year-old man presented with anorexia, nausea and repeated vomiting for 3 days. He also noticed high-coloured urine and pain in the right upper abdomen for 2 days. Investigation reveals:

- Haemoglobin (Hb) 14 g/dL, white blood cells (WBCs) 3900/cmm, polymorphs 46%, lymphocytes 50%, eosinophil 4%.
- Serum bilirubin: 7.2 mg/dL (normal up to 1.2 mg/dL).
- SGPT: 800 IU/L (normal <20 IU/L).
- Serum alkaline phosphatase: 95 IU/L (normal 20–100 IU/L).

Q: Mention **two physical signs** you should look for.

A: As follows:

- Jaundice.
- Liver (enlarged and tender).

Q: What is the likely **diagnosis**?

A: Acute viral hepatitis.

Q: Mention **one investigation** that is helpful to see the prognosis.

A: Prothrombin time.

Q: Mention **two other investigations**.

A: As follows:

- Viral screening (HBsAg, anti-HAV, anti-HEV).
- USG of the hepatobiliary system.

Q: Mention **two other differential diagnoses**.

A: As follows:

- Drug-induced hepatitis.
- Leptospirosis.

Q: Mention **two complications**.

A: As follows:

- Acute fulminating hepatic failure.
- Chronic liver disease.

Q: Mention **one serious complication**.

A: Acute fulminating hepatic failure.

N.B. With the aforementioned history and high bilirubin, high SGPT is suggestive of acute viral hepatitis. Alkaline phosphatase is normal or slightly high. Usually, hepatitis B and C infection may cause chronic liver disease. Hepatitis E may be serious if associated with pregnancy.

Case 03: Haemolytic Jaundice

A 20-year-old man presented with high-coloured urine and yellow colouration of the whole body. There is no history of anorexia, nausea or vomiting. Laboratory investigations reveal:

- Hb 8 g/dL, WBCs 6600/cmm, polymorphs 65%, lymphocytes 20%, platelet count 180,000/cmm, erythrocyte sedimentation rate (ESR) 95 mm in the first hour.
- Serum bilirubin: 3.2 mg/dL (normal up to 1.2 mg/dL).
- SGPT: 45 IU/L (normal <20 IU/L).
- Serum alkaline phosphatase: 250 IU/L (normal 20–100 IU/L).

Q: What is the likely **diagnosis**?

A: Haemolytic jaundice.

Q: Mention **three important physical findings** in this patient.

A: As follows:

- Anaemia.
- Jaundice.
- Splenomegaly.

Q: Mention **two haematological investigations** to find out the cause.

A: As follows:

- Peripheral blood film (PBF) (shows microcytic hypochromic anaemia in hereditary haemolytic anaemia, macrocytic in autoimmune anaemia).
- Reticulocyte count (by supravital stain): High.

Q: Mention **two further investigations** to confirm your diagnosis.

A: As follows:

- Hb electrophoresis (to see the type of hereditary haemolytic anaemia).
- Coombs test (to exclude autoimmune haemolytic anaemia).

N.B. Anaemia with high bilirubin but normal hepatic enzyme (normal SGPT, alkaline phosphatase) is highly suggestive of haemolytic anaemia. Mostly, it may be a result of hereditary haemolytic anaemia (e.g., thalassaemia major) or autoimmune haemolytic anaemia.

Case 04: Gilbert Syndrome

A young student presented with weakness, anorexia, nausea and high-coloured urine. He was suffering from sore throat 10 days back. There is a history of similar attack. On examination: anaemia—mild, jaundice—mild, liver—just palpable, nontender. Investigations show:

- Complete blood cell (CBC) count: Hb 10.2 g/dL, ESR 32 mm in the first hour, WBCs 9900/cmm, polymorphs 61%, lymphocytes 35%, monocytes 4%.
- Reticulocyte count: 0.7% (normal 0.2%–2%).
- Total bilirubin: 52 μ mol/L (normal <17 μ mol/L).
- Alanine transaminase (ALT) (SGPT): 15 IU/L (normal <20 IU/L).
- Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase [SGOT]): 21 IU/L (normal <25 IU/L).
- Alkaline phosphatase: 42 IU/L (normal 20–100 IU/L).
- USG of the abdomen: Mild hepatomegaly.

Q: What is the likely **diagnosis**?

A: Gilbert syndrome.

Q: Suggest **two investigations**.

A: As follows:

- 48 hours, 400-kcal restriction test.
- 50 mg nicotine i.v. (there is a rise in the level of bilirubin).

Q: What **treatment** should be given to this patient?

A: As follows:

- Reassurance.
- Prolonged fasting should be avoided.
- Therapeutic trial with phenobarbitone 60 mg t.d.s.

***N.B.** Recurrent jaundice but the presence of normal liver enzymes in a young patient is highly suggestive of Gilbert syndrome. It is a type of unconjugated nonhaemolytic hyperbilirubinaemia and occurs in 2%–7% of normal individuals; some cases are inherited as autosomal dominant. Most patients remain asymptomatic. Jaundice is usually mild and occurs intermittently during infection or prolonged fasting. Liver enzymes are normal, and there are no signs of liver disease. It is as a result of defect in the uptake of bilirubin by the liver and also there is a deficiency of UDP-glucuronyl transferase activity, which conjugates bilirubin with glucuronic acid. Liver biopsy is normal. Other causes of nonhaemolytic hyperbilirubinaemia are Crigler–Najjar syndrome (types 1 and 2), Dubin–Johnson syndrome (liver is black as a result of increased deposition of lipofuscin and melanin) and Rotor syndrome.*

NEPHROLOGY

Case 01: Acute Glomerulonephritis

A 12-year-old boy presented with scanty micturition and puffy face. Urine examination shows:

- Colour: Smoky.
- Albumin +.
- Pus cells: 0–2/high powered field (HPF).
- RBCs: 20–30/HPF.
- RBC cast: Present.

Q: What is the probable **diagnosis**?

A: Acute glomerulonephritis.

Q: Mention **one history** you should take.

A: A history of sore throat 1–3 weeks back.

Q: Write down **three clinical signs** you should look for.

A: As follows:

- Periorbital oedema.
- Blood pressure (BP) (high).
- Lungs (bilateral basal crepitation: Indicates acute left ventricular failure [LVF]).

Q: Write **four further investigations**.

A: As follows:

- Blood urea and serum creatinine.
- Serum electrolytes.
- USG of the renal system.
- X-ray chest (PA view).

Q: Mention **two complications**.

A: As follows:

- Acute LVF.
- Acute renal failure (ARF).

Q: Write down the **principles of management**.

A: As follows:

- Salt and fluid restriction.
- Diuretic such as frusemide.
- Antibiotic: Penicillin.

***N.B.** A history of sore throat, followed by scanty, smoky urine associated with a puffy face and periorbital oedema, is highly suggestive of acute glomerulonephritis (usually poststreptococcal glomerulonephritis).*

Case 02: Nephrotic Syndrome

A 7-year-old girl presented with swelling of the whole body with scanty micturition for 10 days. Her urine examination reveals:

- Colour: Straw.
- Albumin +++.
- RBC: Nil.
- Pus cells: 0–2/HPF.
- Fatty cast present.

Q: What is the likely **diagnosis**?

A: Nephrotic syndrome.

Q: Mention **three investigations**.

A: As follows:

- Serum total protein and albumin.
- 24-hour urinary protein (>3 g).
- Serum lipid profile (there are high cholesterol and triglyceride levels).

Q: Mention **one drug** you think that should be given to this patient.

A: Prednisolone.

N.B. Generalized oedema, massive proteinuria and hypoalbuminaemia are suggestive of nephrotic syndrome. Commonest cause is minimal-change disease in children and membranous or proliferative glomerulonephritis in adults. Prognosis is better in children, but there may be relapse.

Case 03: Sterile Pyuria

A 40-year-old man presented with a low-grade fever, weakness, loss of appetite and difficulty in micturition. Urine examination shows:

- Albumin +.
- RBCs: 5–6/HPF.
- Pus cells: 50–60/HPF.
- Culture: No growth.

Q: What does the urine report **show**?

A: Sterile pyuria.

Q: Mention **three causes**.

A: As follows:

- Renal tuberculosis.
- Partially treated urinary tract infection.
- Nongonococcal urethritis.
- Analgesic nephropathy.
- Tubulointerstitial nephritis.
- Prostatitis.
- Bilharziasis.

Q: Mention **two commonest causes**.

A: As follows:

- Renal tuberculosis.
- Partially treated urinary tract infection.

Q: Mention **four further investigations**.

A: As follows:

- Urine for acid-fast bacteria (AFB) and mycobacterial culture.
- USG of the renal system.
- Tuberculin test.
- Chest X-ray.

N.B. Presence of pus cells in the urine but sterile on culture is called sterile pyuria. Tuberculosis of the renal system is the likely cause.

Case 04: Acute Pyelonephritis

A 30-year-old woman presented with high temperature, anorexia, nausea, vomiting, frequency of micturition and pain in the lumbar region. Urine examination shows:

- Albumin +.
- RBCs few.
- Pus cells plenty.

Q: What is the likely **diagnosis**?

A: Acute pyelonephritis.

Q: Mention **one investigation** to confirm the diagnosis.

A: Urine culture and sensitivity.

N.B. Any patient with frequency, burning or difficulty in micturition associated with high temperature has a suspicion of acute pyelonephritis. Treatment should be given according to culture and sensitivity of urine.

Case 05: Acute Interstitial Nephritis with ARF as a Result of Cefixime

A 60-year-old man presented with fever, headache, dry cough, frequency of micturition and weakness for 10 days. Cefixime was given by a general practitioner. After 5 days, the patient had complaints of scanty urine, puffiness of the face, swelling of legs, polyarthralgia and multiple skin rashes. Investigations reveal:

- Full blood count: Hb 10.9 g/dL, WBCs 11,200/cmm, polymorphs 64%, lymphocytes 28%, eosinophils 8%, ESR 110 mm in the first hour, platelets 175,000/cmm.
- Urine: Pus cells—plenty, proteinuria (++); total protein 1 g/24 h.
- Urea: 19 mmol/L (normal 2.5–6.6 mmol/L).
- Creatinine: 833 μ mol/L (normal 60–120 mmol/L).
- Serum electrolytes: Sodium 130 mmol/L, chloride 90 mmol/L, potassium 6.1 mmol/L, bicarbonate 17 mmol/L.

Q: What is your **diagnosis**?

A: Acute interstitial nephritis with ARF as a result of cefixime.

Q: Suggest **two further investigations**.

A: USG of kidney, renal biopsy.

Q: How to **confirm** the diagnosis?

A: Renal biopsy.

Q: How to **manage** this case?

A: As follows:

- Offending drug should be stopped.
- Prednisolone.
- Dialysis for ARF.

N.B. This patient presents with fever, skin rash, eosinophilia and renal impairment shortly after antibiotic therapy. These findings are consistent with acute interstitial nephritis. It is an acute inflammation of tubular interstitium, probably as a result of hypersensitivity reaction.

NEUROLOGY

Case 01: Tubercular Meningitis

A 25-year-old man presented with fever for 3 weeks and disorientation for 3 days. Cerebrospinal fluid (CSF) study shows:

- Pressure: High.
- Colour: Clear.
- Cytology: Total WBCs 350/cmm, neutrophils 5%, lymphocytes 95%, no RBCs.
- Biochemistry: Protein 300 mg/dL (normal up to 40 mg/dL), sugar 50 mg/dL (low).
- Microbiology: No organisms were found on the Gram stain.

Q: What is the likely **diagnosis**?

A: Tubercular meningitis.

Q: Mention **four differential diagnoses**.

A: As follows:

- Viral meningitis.
- Fungal meningitis.
- Sarcoidosis.
- Neurosyphilis or meningovascular syphilis.

Q: Mention **one other CSF investigation** that is helpful for your diagnosis.

A: ADA (adenosine deaminase).

Q: What is the **other CSF finding**?

A: If it is kept overnight, there is a cobweb appearance.

Q: Write down **two important physical signs**.

A: As follows:

- Neck rigidity.
- Kernig sign.

Q: What **four other investigations** will you suggest?

A: As follows:

- CBC count with ESR.
- Tuberculin test.
- Chest X-ray (PA view).
- CT scan of the head.

Q: What is the finding on **fundoscopy**?

A: Choroid tubercle in the retina.

***N.B.** History of a low-grade fever, weight loss and anorexia, along with signs of meningitis and typical CSF findings (high lymphocyte, high protein and low sugar levels), is highly suggestive of tuberculous meningitis. It should be treated with standard antitubercular therapy for at least 9 months plus prednisolone 60 mg for 3 weeks and then taper. Complications (e.g., cranial nerve palsy, hydrocephalus, syndrome of inappropriate antidiuretic hormone secretion [SIADH], seizure) may occur.*

Case 02: Pyogenic Meningitis

A 19-year-old man presented with a high-grade fever for 2 days and disorientation for 4 hours. Neck rigidity and Kernig sign were present. CSF examination shows:

- Colour: Turbid.
- Pressure: Increased.
- Biochemistry: Protein 190 mg/dL, sugar 16 mg/dL, chloride 670 mg/dL.
- Cytology: Total cells 6200/cmm, polymorphs 96%, lymphocytes 4%.

Q: What is the likely **diagnosis**?

A: Pyogenic meningitis.

Q: What are the **causes** of bacterial meningitis?

A: As follows:

1. Neonates: Gram-negative bacilli (*Escherichia coli*, *Proteus*), group B streptococci, *Listeria monocytogenes*.
2. Preschool-aged children: *Haemophilus influenzae*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Mycobacterium tuberculosis*.
3. Older children and adults: *N. meningitidis*, *S. pneumoniae*, *L. monocytogenes*, *M. tuberculosis*, *Staphylococcus aureus* (skull fracture), *H. influenzae*.

Q: What is the **commonest organism**?

A: *N. meningitidis* (also called meningococcus).

Q: What are the **complications**?

A: As follows:

- Brain abscess.
- Hydrocephalus.
- Cranial nerve palsy.

Q: What other **physical findings** will you look in the body?

A: Skin rash such as petechia or purpura, which indicate meningococcal septicaemia.

Q: If the patient develops **shock**, what is the likely cause?

A: Bilateral adrenal haemorrhage (Waterhouse–Friderichsen syndrome).

Q: What would you look for **before doing lumbar puncture**? Why?

A: Fundoscopy is performed to see papilloedema (indicates raised intracranial pressure). If it is present, then lumbar puncture should be avoided because there may be herniation of cerebellar tonsils through foramen magnum, which compresses the vital centre in medulla oblongata and causes sudden death.

N.B. In any patient with high fever, headache, nausea, vomiting and photophobia with signs of meningism, it indicates pyogenic meningitis.

Case 03: Acute Viral Meningitis

A 24-year-old man presented with fever, headache, nausea and vomiting for 5 days. Neck rigidity and Kernig sign were present. CSF examination shows:

- Colour: Clear.
- Pressure: Increased.
- Biochemistry: Protein 60 mg/dL, sugar 50 mg/dL.
- Cytology: Total cells 100/cmm, polymorphs 2%, lymphocytes 98%.

Q: What is the likely diagnosis?

A: Acute viral meningitis.

Q: What are the common organisms?

A: Enteroviruses such as echovirus and coxsackievirus are the commonest.

N.B. Low-grade fever, headache, nausea, vomiting and CSF findings—clear, slightly high protein with normal glucose and chloride, and high lymphocytes are suggestive of viral encephalitis. There are usually no serious sequelae unless encephalitis is present.

Case 04: Subarachnoid Haemorrhage

A 45-year-old man presented with a sudden, severe occipital headache, followed by unconsciousness. Neck rigidity and Kernig sign were present. CSF shows:

- Colour: Red (frank blood).
- Pressure: Increased.
- Biochemistry: Protein 100 mg/dL, sugar 60 mg/dL.
- Cytology: Plenty of RBCs, polymorphs 60%, lymphocytes 40%.

Q: What is the likely diagnosis?

A: Subarachnoid haemorrhage.

Q: Mention two causes?

A: As follows:

- Rupture of berry aneurysm.
- Rupture of arteriovenous malformation.

Q: Mention one fundoscopy finding.

A: Subhyaloid haemorrhage.

Q: Suggest one investigation.

A: CT scan of the head.

Q: Mention two other investigations.

A: As follows:

- Magnetic resonance angiography (MRA).
- Digital subtraction angiogram (DSA).
- Cerebral angiography.

Q: Mention two **causes** of haemorrhagic CSF.

A: As follows:

- Subarachnoid haemorrhage.
- Trauma.
- Bleeding disorders such as haemophilia, Christmas disease.

N.B. Sudden, severe thunderclap headache, followed by unconsciousness, is highly suggestive of subarachnoid haemorrhage. Control of hypertension, administration of nimodipine and surgical obliteration of the aneurysm by clipping are the mainstay of treatment.

HAEMATOLOGY

Case 01: Acute Leukaemia

A 35-year-old woman presented with the following blood report:

1. Hb 6 g/dL, ESR 70 mm in the first hour.
2. WBCs: $50 \times 10^9/\text{cmm}$.
 - Neutrophils: 35%.
 - Lymphocytes: 28%.
 - Monocytes: 03%.
 - Eosinophils: 05%.
 - Atypical cells: 29%.
3. Platelets: $100 \times 10^9/\text{cmm}$.

Q: What are the **abnormalities** in this blood profile?

A: Anaemia, leucocytosis with atypical cells, thrombocytopaenia, high ESR.

Q: What is the likely **diagnosis**?

A: Acute leukaemia.

Q: Mention one further **investigation**.

A: Bone marrow study.

N.B. Presence of atypical cells with a high WBC count is suggestive of acute leukaemia, which may be either myeloid or lymphoblastic. Blast cells may be present.

Case 01: Chronic Myeloid Leukaemia (CML)

A 45-year-old man presented with weakness, loss of appetite and heaviness in the abdomen for 3 months. Laboratory investigation reveals:

1. Hb 9 g/dL, WBCs 150,000/cmm, polymorphs 45%, lymphocytes 8%, myelocytes 22%, metamyelocytes 14%, myeloblasts 3%, basophils 8%, platelets 210,000/cmm, ESR 90 mm in the first hour.
2. PBF: Normocytic normochromic anaemia.

Q: What are the **abnormalities** in this blood profile?

A: Anaemia, leucocytosis with myelocyte and metamyelocyte, few blast cells, high basophils and high ESR.

Q: What is your **diagnosis**?

A: Chronic myeloid leukaemia.

Q: What is the **cause** of abdominal discomfort?

A: Splenomegaly, which may be huge.

Q: What **investigation** do you suggest?

A: As follows:

- Bone marrow study.
- Cytogenetic analysis for Philadelphia chromosome.
- RNA analysis to see the presence of BCR–ABL gene product.
- Leucocyte alkaline phosphatase (LAP) score (decreases).

Q: What are the **therapies** that may be used to cure this condition?

A: Bone marrow transplantation, imatinib and α -interferon.

N.B. In a middle-aged patient with a huge splenomegaly and the presence of anaemia, leucocytosis with myelocyte and metamyelocyte, few blast cells, high basophils, high ESR is suspected to have CML. Blastic crisis, myelofibrosis may occur. CML may be associated with a low LAP score, high uric acid, high vitamin B₁₂ and high lactic dehydrogenase (LDH).

Case 03: Multiple Myeloma

A 65-year-old man presented with generalized body ache for the last 3 months. Laboratory investigation reveals:

- Hb 8 g/dL, WBCs normal, platelets 200,000/cmm.
- ESR: 115 mm in the first hour.
- PBF: Normocytic normochromic anaemia with increased rouleaux formation.
- Blood Ca²⁺: High.

Q: What is the likely **diagnosis**?

A: Multiple myeloma.

Q: Write down two important **investigations** to confirm the diagnosis.

A: As follows:

- Bone marrow study (shows atypical plasma cells).
- Serum protein electrophoresis or immunoelectrophoresis.
- X-ray of the skull (shows multiple lytic lesions).

Q: Write down three **complications**.

A: As follows:

- Pathological fracture of the bone.
- Renal failure.
- Hyperviscosity syndrome.
- Bone marrow failure.
- Repeated infection.

Q: Mention one **drug** that may be curative.

A: Bortezomib.

N.B. Elderly patients may present with generalized body ache, unexplained anaemia, repeated infection, spontaneous fracture, hyperviscosity syndrome, bleeding disorder and renal failure in multiple myeloma. Blood examination shows very high ESR with marked rouleaux formation in PBF. Bone marrow study shows the presence of atypical plasma cells (usually >20%). Urine shows Bence–Jones proteinuria.

Case 04: Pancytopenia

A 40-year-old man presented with a generalized weakness and gum bleeding for 2 months. Investigation reveals:

- Hb: 7 g/dL.
- WBCs: 15,000/cmm.
- Neutrophils: 16%.
- Lymphocytes: 81%.
- Platelets: 20,000/cmm.
- ESR: 70 mm in the first hour.

Q: What is the haematological **diagnosis**?

A: Pancytopenia.

Q: Mention three **causes**.

A: As follows:

- Aplastic anaemia.
- Hypersplenism.
- Megaloblastic anaemia.
- Aleukaemic leukaemia.
- Paroxysmal nocturnal haemoglobinuria.

Q: Mention one **investigation** to confirm the diagnosis?

A: Bone marrow study.

N.B. Anaemia, leucopenia and thrombocytopenia indicate pancytopenia. The commonest cause is aplastic anaemia. The causes of aplastic anaemia are primary idiopathic, secondary (bone marrow infiltration, multiple myeloma, drugs, radiotherapy etc.).

Case 05: Hypochromic Microcytic Anaemia

A 29-year-old woman presented with weakness, palpitation and shortness of breath on exertion. Laboratory investigation reveals:

- Hb 8.5 mg/dL.
- RBC, WBC and platelet counts are within normal limits.
- PBF shows hypochromia.
- Mean cell volume (MCV): 65 fL (normal >80 fL).

Q: What is haematological **diagnosis**?

A: Hypochromic microcytic anaemia.

Q: Mention four **causes**.

A: As follows:

- Iron-deficiency anaemia.
- β -Thalassaemia.
- Sideroblastic anaemia.
- Anaemia of chronic disorder.

Q: Which one is the more likely **diagnosis** in this patient?

A: Iron-deficiency anaemia.

Q: What is the commonest **cause** of iron-deficiency anaemia?

A: Bleeding (menorrhagia, haemorrhoid).

Q: What **history** would you like to take in this female patient?

A: History of menorrhagia.

Q: What further **investigation** will you do?

A: As follows:

- Iron profile (serum iron, serum ferritin, total iron binding capacity [TIBC]).
- Hb electrophoresis.
- Bone marrow study.

N.B. Microcytic hypochromic blood profile with a history of blood loss suggests iron-deficiency anaemia. Serum iron and ferritin will be low and TIBC will be high. Treatment includes correction of anaemia by blood transfusion, iron therapy for 3–6 months (to replenish the store) and treatment of primary cause.

Case 06: β -Thalassaemia Major

A 15-year-old girl presented with weakness, abdominal distension and loss of appetite. Examination of the abdomen reveals huge splenomegaly and mild hepatomegaly. Laboratory results show:

- Hb 7%, WBCs 7200/cmm, neutrophils 62%, lymphocytes 23%, platelets 230,000/cmm.
- Reticulocytes: 10%.
- MCV: 69 fL (normal >80).
- Serum bilirubin: 3.1 mg/dL.

Q: What is the likely **diagnosis**?

A: β -Thalassaemia major.

Q: What is the **triad of signs** in this condition?

A: As follows:

- Anaemia.
- Jaundice.
- Splenomegaly.

Q: What **history** is important in such a condition?

A: Family history of such an illness.

Q: What **physical signs** will you look for?

A: Anaemia, jaundice, frontal and parietal bossing, mongoloid facies and splenomegaly.

Q: What **investigation** will you do to confirm the diagnosis?

A: Hb electrophoresis.

Q: What **treatment** should be given?

A: As follows:

- Blood transfusion to keep Hb above 10 g/dL, usually every 4 months (life span of RBCs is 4 months).
- Folic acid supplementation daily.
- Iron-containing drugs and diet should be avoided.
- Desferrioxamine to prevent transfusion haemosiderosis.
- Erythropoietin and hydroxyurea may be given.
- Specific treatment: Allogenic bone marrow transplantation.
- If huge splenomegaly with features of hypersplenism: Splenectomy may be done.

N.B. Presence of microcytic hypochromic anaemia with a high reticulocyte count, jaundice and splenomegaly in a young patient indicates hereditary haemolytic anaemia, most commonly β -thalassaemia major. Other common hereditary haemolytic anaemia—HbE disease, thalassaemia E disease (double heterozygous).

Case 07: Macrocytic Anaemia

A 50-year-old woman presented with weakness and anorexia for 3 months. Her laboratory investigations reveal:

- Hb 8%, WBCs 6700/cmm, neutrophils 65%, lymphocytes 25%, platelets 210,000/cmm.
- Reticulocytes: 1%.
- MCV: 112 fL (normal up to 96 fL).
- PBF shows macrocytosis and hypersegmented neutrophils.
- Serum bilirubin: 1.0 mg/dL.

Q: What is the haematological **diagnosis**?

A: Macrocytic anaemia.

Q: What are the **causes** of macrocytosis?

A: As follows:

- Megaloblastic anaemia (as a result of vitamin B₁₂ or folic acid deficiency).
- Hypothyroidism.
- Chronic liver disease.
- Chronic alcoholism.
- Haemolysis.
- Azathioprine therapy.

Q: What should be the next **investigation**?

A: Bone marrow study.

Q: What are the **findings in bone marrow** study and how would you interpret them?

A: As follows:

- If macrocytosis is associated with megaloblasts in bone marrow: The diagnosis is megaloblastic anaemia.
- If macrocytosis is associated with normoblastic bone marrow: The causes are hypothyroidism, chronic liver disease, chronic alcoholism, haemolysis, azathioprine therapy etc.

Q: What other **investigations** do you suggest?

A: Serum vitamin B₁₂ and folic acid assay.

N.B. Anaemia with high MCV indicates macrocytic anaemia. Most common cause is megaloblastic anaemia as a result of vitamin B₁₂ or folic acid deficiency.

Case 08: Leukemoid Reaction

A 60-year-old woman presented with fever, cough and weight loss. She was suffering from breast cancer, which was treated by mastectomy and chemotherapy. Her blood profile shows:

- Hb 11.4 g/dL, WBCs 23,700/cmm, polymorphs 82%, lymphocytes 6%, metamyelocytes 3%, myelocytes 3%, promyelocytes 1%, myeloblast 1%, erythroblast 4%, platelets 180,000/cmm.
- ESR: 10 mm in the first hour.
- Chest X-ray: Absent left breast shadow.

Q: What is the haematological **diagnosis**?

A: Leukemoid reaction.

Q: What is the likely **cause**?

A: Bone marrow infiltration from carcinoma of the breast.

Q: Mention one further **investigation** to confirm your diagnosis?

A: Bone marrow study.

N.B. Leukemoid reaction means that the peripheral blood profile resembles leukaemia, but there is no leukaemia. It may be myeloid or lymphatic. Causes of myeloid leukemoid reaction are leucoerythroblastic anaemia, infection, malignancy and acute haemolysis (LIMA). Causes of lymphatic leukemoid reaction are viral (infectious mononucleosis, cytomegalovirus infection, measles, chickenpox), whooping cough and, rarely, tuberculosis and carcinoma.

Case 09: Leucoerythroblastic Anaemia

A 65-year-old woman presented with pain in the epigastrium, loss of appetite, fever, generalized body ache, night sweating, occasional headache, dizziness and weight loss for 3 months. She was pale and emaciated. There was a massive splenomegaly. Investigations reveal:

- Hb 9.1 g/dL, WBCs 18,500/cmm, polymorphs 60%, lymphocytes 28%, myelocytes 6%, metamyelocytes 2%, myeloblasts 1%, erythroblast 3%, ESR 93 mm in the first hour, platelets 665,000/cmm.
- Liver function tests: Serum bilirubin 28 µmol/L, SGPT 38 IU/L, alkaline phosphatase 200 IU/L.
- Chest X-ray: Normal.

Q: What is the haematological diagnosis?

A: Leucoerythroblastic anaemia.

Q: What is the likely diagnosis?

A: Myelofibrosis.

Q: What additional findings may be seen in the blood film?

A: Teardrop poikilocytes.

Q: What are the other causes of such a blood profile?

A: As follows:

- Secondary deposits in bone marrow.
- Lymphoma.
- Multiple myeloma.
- Active haemolytic anaemia.

Q: Suggest two other tests.

A: As follows:

- Bone marrow study: May be dry tap. Trephine biopsy is needed, which shows increased megakaryocyte, increased reticulin and fibrous tissue.
- LAP score: High.

Q: Mention one dangerous complication.

A: Transformation to acute myeloid leukaemia (AML) (10%–20% of cases).

Q: What treatment should be given?

A: As follows:

- Blood transfusion.
- Folic acid supplementation.
- Hydroxycarbamide (hydroxyurea) may be given.
- In young patients, bone marrow transplantation is required.
- Radiotherapy for a huge spleen.
- If evidence of hypersplenism and a huge spleen with pressure symptoms, splenectomy may be necessary.

N.B. In any elderly patient with a huge splenomegaly and leucoerythroblastic blood profile, the likely cause is myelofibrosis. PBF shows teardrop or pear-shaped poikilocytes. Myelofibrosis is a disorder of an unknown cause, characterized by bone marrow fibrosis, extramedullary haemopoiesis and leucoerythroblastic blood profile as a result of neoplastic proliferation of primitive stem cells. It is common above 50 years of age. There may be peptic ulcer, pruritus after hot bath, gout etc.

Case 10: Blastic Crisis in CML

A 53-year-old man had a diagnosis of chronic granulocytic leukaemia. He underwent chemotherapy and responded well. Three years later, the patient presented with complaints of severe weakness, loss of weight, lethargy, epistaxis and pain in the left upper abdomen. Investigations show:

- Hb 7.5 g/dL, WBCs 12,800/cmm, platelets 100,000/cmm, RBCs 2.8 million/cmm, ESR 85 mm in the first hour.
- Differential count: Neutrophils 34%, basophils 8%, lymphocytes 6%, myeloblasts 40%, myelocytes 10%, metamyelocytes 2%.

Q: What is the **diagnosis**?

A: Blastic crisis in CML

Q: What is the cause of **abdominal pain**?

A: Splenic infarction.

Q: Suggest one **investigation** to confirm your diagnosis.

A: Bone marrow study.

N.B. Appearance of an increased number of blast cells in PBF in a patient with CML suggests blastic crisis. It may be myeloid or lymphatic.

Case 11: Idiopathic Thrombocytopenic Purpura (ITP)

A 13-year-old girl presented with several small bruises on her arms and legs 9 days after recovering from a viral fever. Investigations reveal:

- Full blood cell count: Hb 11.3 g/dL, WBCs 10,700/cmm, polymorphs 59%, lymphocytes 38%, ESR 60 mm in the first hour, platelet count 80,000/cmm.
- Blood film: Normocytic and normochromic.
- Chest X-ray: Normal.

Q: What is the likely **diagnosis**?

A: Idiopathic thrombocytopenic purpura.

Q: Suggest two diagnostically useful **investigations**.

A: Bone marrow study and antiplatelet antibody.

Q: What disease should be **excluded** in such a finding?

A: Systemic lupus erythematosus (SLE).

Q: What **treatment** should be given?

A: In children, it is usually self-limiting. If no improvement, then:

- Prednisolone (2 mg/kg)
- Intravenous (IV) immunoglobulin if persistent bleeding.
- Platelet transfusion if persistent bleeding.
- If thrombocytopaenia persists for more than 6 months, it is chronic. In that case, splenectomy should be considered.

N.B. Purpuric spot in a patient with a recent history of viral fever, associated with a low platelet count and increased megakaryocytes in bone marrow, is suggestive of ITP. In ITP, low platelets, increased megakaryocytes in bone marrow, prolonged bleeding time and normal clotting time are common. There may be antiplatelet antibody and anticardiolipin antibody. Initially, SLE and antiphospholipid syndrome may present as in ITP.

Case 12: Polycythaemia Rubra Vera (PRV)

A 41-year-old man presented with frequent headache, dizziness, lack of concentration, pruritus and heaviness in the left upper abdomen for 3 months. Laboratory investigations reveal:

- Hb 17.6 g/dL, WBCs 21,000/cmm, polymorphs 83%, lymphocytes 15%, eosinophils 2%, RBCs 8.2 million/cmm, platelets 850,000/cmm, ESR 1 mm in the first hour.
- Packed cell volume (PCV): 65% (normal up to 45%).
- Random blood sugar (RBS): 7.2 mmol/L.
- Chest X-ray: Normal.

Q: What is your **diagnosis**?

A: PRV.

Q: Suggest one **investigation**.

A: Measurement of red cell mass (increased).

Q: Suggest one **treatment**.

A: Venesection.

Q: What **drugs** can be used?

A: Radioactive phosphorus, hydroxyurea, interferon.

Q: Mention four **complications**.

A: As follows:

- AML.
- Thromboembolism (cerebral, coronary).
- Hypertension.
- Gout.
- Peptic ulcer.
- Myelofibrosis.

N.B. This patient has high Hb and RBCs, as well as high PCV, which suggest polycythaemia. High WBC and platelet counts associated with splenomegaly are all in favour of PRV. Red cell volume is high in PRV. There is increased LAP score, vitamin B₁₂ and uric acid (may cause gout). Bone marrow shows hypercellular with increased megakaryocytes.

Case 13: Disseminated Intravascular Coagulation (DIC)

A 29-year-old woman was admitted to the hospital with complaints of blood loss PV (per vaginam) and a high-grade, continuous fever following a self-induced abortion. She looked toxic, anaemia—severe, BP 80/60 mm Hg, pulse 124/min, temperature 39.6°C. Lower abdomen—very tender. Investigations reveal:

- Full blood count: Hb 5.0 g/dL, WBCs 28,700/cmm, polymorphs 87%, lymphocytes 13%, platelets 30,000/cmm, ESR 85 mm in the first hour.
- PBF: Microcytic, hypochromic and fragmented RBCs.
- Prothrombin time: 30 seconds (control 12).
- Activated partial thromboplastin time (APTT): 60 seconds (control 32).
- Fibrinogen: 0.05 g/L (1.5–4.0 g).

Q: What is the main **diagnosis** in this blood disorder?

A: Disseminated intravascular coagulation.

Q: Mention four **abnormalities** in this blood profile.

A: DIC with microangiopathic haemolytic anaemia with iron-deficiency anaemia along with septicaemia.

Q: Give three possible **causes** of haematological abnormality.

A: Septicaemia, retained product of conception or amniotic fluid embolism.

N.B. DIC is a haemorrhagic disorder in which diffuse intravascular clotting causes a haemostatic defect resulting from utilization of coagulation factor and platelets in the clotting process. There is secondary activation of fibrinolysis, leading to production of fibrin degradation products (FDP). The consequence of these changes is a mixture of initial thrombosis, followed by bleeding tendency as a result of consumption of coagulation factors and fibrinolytic activity.

RESPIRATORY

Case 01: Interstitial Lung Disease

A 46-year-old woman was admitted to the emergency department with shortness of breath, cough, swelling in both feet and extreme weakness. Respiratory function tests reveal:

- Vital capacity: 2.0 L (predicted 2.4–3.6 L).
- Forced expiratory volume in 1 second (FEV₁): 2.1 L (predicted 2.25–3.25 L).
- Transfer factor: 4.1 L (predicted 5.8–8.7 L).
- Residual volume (RV): 1.1 L (predicted 1.55–2.32 L).

Q: What pulmonary **defect** is present?

A: Restrictive lung disease.

Q: What is the likely **diagnosis** with the aforementioned findings?

A: Interstitial lung disease.

Q: Suggest five **investigations** to find out the cause.

A: As follows:

- Chest X-ray.
- CT scan of the chest.
- ABG (arterial blood gas) analysis.
- Bronchoscopy and bronchoalveolar lavage.
- Transbronchial or open lung biopsy.

Q: What are the **causes** of restrictive lung disease?

A: As follows:

- Sarcoidosis.
- Diffuse parenchymal lung disease (DPLD).
- Ankylosing spondylitis.

***N.B.** In restrictive lung disease, both forced vital capacity (FVC) and FEV₁ are proportionately reduced, but the ratio of these two is normal. Total lung capacity (TLC) is reduced, and RV is reduced or normal. Carbon monoxide (CO) transfer factor is also low.*

Case 02: Emphysema

A woman of 42 years, housewife, had been suffering from breathlessness, occasional dry cough and weight loss for 2 years. Her lung function test shows:

- FVC: 2.00 L (predicted 2.4–3.6 L).
- FEV₁: 1.45 L (predicted 2.25–3.25 L).
- RV: 2.89 L (predicted 1.5–2.32 L).
- Functional Residual Capacity (FRC): 3.56 L (predicted 2.17–3.25 L).
- TLC: 5.89 L (predicted 3.96–5.66 L).
- Transfer factor or Diffusion capacity of Lung for Carbon Monoxide (TLCO or DLCO): 4.7 mmol/min/kPa (predicted 5.8–8.7 L).

Q: What is the **lung function test**?

A: Obstructive airway disease.

Q: What is the most likely **diagnosis**?

A: Emphysema.

Q: Suggest two possible **causes**.

A: α_1 -Antitrypsin deficiency, cigarette smoking.

Q: **Name** two obstructive airway diseases.

A: Chronic obstructive pulmonary disease (COPD) and bronchial asthma.

N.B. In obstructive lung disease, FEV_1 is markedly reduced; FVC is also reduced. The ratio of these two is also reduced. CO transfer factor is low. RV and TLC are high.

ENDOCRINE

Case 01: Primary Hyperparathyroidism

A 52-year-old woman presented with frequency of micturition, extreme weakness, loss of appetite, constipation, abdominal pain and weight loss for 7 months. Investigations reveal:

- Full blood count: Hb 10.6 g/dL, WBCs 8900/cmm, polymorphs 55%, lymphocytes 43%, monocytes 2%, ESR 90 mm in the first hour.
- Plain X-ray KUB (kidneys, ureters, bladder): Nephrocalcinosis.
- USG of the abdomen: Calcification in both kidneys.
- Urine: Protein (+), few pus cells.
- RBS: 6.9 mmol/L.
- Creatinine: 1.4 mg/dL.
- Serum electrolytes: Sodium 139 mmol/L, chloride 110 mmol/L, potassium 3.6 mmol/L, bicarbonate 22 mmol/L.

Q: What is the likely **diagnosis**?

A: Primary hyperparathyroidism.

Q: Suggest **five investigations** to confirm your diagnosis.

A: As follows:

- Serum calcium, phosphate and alkaline phosphatase.
- Parathyroid hormone assay.
- Hydrocortisone suppression test.
- X-ray of the hand (to see subperiosteal erosion in the medial side of phalanges) and X-ray of the skull (to see pepper-pot appearance).
- USG or CT scan of the neck (parathyroid adenoma or hyperplasia).
- Other test: Thallium/technetium subtraction scan of the thyroid and parathyroid glands.

Q: What single **treatment** should be given immediately?

A: Plenty of fluid (infusion of normal saline 4–6 L daily) for hypercalcaemia.

N.B. The aforementioned symptoms associated with hypercalcaemia and nephrocalcinosis indicate hyperparathyroidism. It may be primary (as a result of adenoma, hyperplasia or carcinoma of the parathyroid), secondary (chronic renal failure, malabsorption, rickets or osteomalacia) or tertiary (autonomous from secondary). In mild and asymptomatic cases, follow-up is done. Total parathyroidectomy with transplantation of the parathyroid in the forearm muscles is done in primary hyperparathyroidism. Surgery is also required for tertiary hyperparathyroidism. Treatment of secondary causes should be done.

Case 02: Thyrotoxicosis as a Result of Graves Disease

A 32-year-old woman presented with bilateral proptosis, gritty sensation and discomfort in both eyes, palpitation and weight loss. Investigation reveals:

- Serum FT₃: 9.0 pmol/L (normal 1.3–3.5 pmol/L).
- Serum FT₄: 215 pmol/L (normal 70–160 pmol/L).
- Thyroid-stimulating hormone (TSH): 0.04 mIU/L (normal 0.5–5.1 mIU/L).

Q: What is your **diagnosis**?

A: Thyrotoxicosis as a result of Graves disease.

Q: Write down two other **causes** of such investigation findings.

A: As follows:

- Toxic multinodular goitre.
- Toxic adenoma.

Q: Write down **two important findings** by examining the nervous system of this patient.

A: As follows:

- Tremor of the outstretched hand.
- Jerks, which are exaggerated.

Q: Write down four other important **investigations**.

A: As follows:

- Radioiodine uptake test.
- Thyroid scan.
- USG of the neck.
- TSH receptor antibody (TRAb) test.

Q: Write down the modalities of **treatment**.

A: As follows:

- Antithyroid drugs: Carbimazole or propylthiouracil.
- Radioactive iodine therapy.
- Thyroid surgery.

N.B. Graves disease is characterized by diffuse goitre, exophthalmos and dermopathy. The natural history of Graves disease is hyperthyroidism, followed by euthyroid and, later, hypothyroidism. TRAb is high. Antimicrosomal (antiperoxidase) and antithyroglobulin antibody may be present in low titre.

Case 03: Primary Hypothyroidism

A 35-year-old woman presented with a generalized weakness and weight gain. Her thyroid function test reveals:

- Serum FT₃: 2 pmol/L (normal 1.3–3.5 pmol/L).
- Serum FT₄: 7 pmol/L (normal 70–160 pmol/L).
- TSH: 35 mIU/L (normal 0.5–5.1 mIU/L).

Q: What is the most likely clinical **diagnosis**?

A: Primary hypothyroidism.

Q: Mention four important **clinical signs** of this patient.

A: As follows:

- Hoarseness or croaky voice.
- Puffiness of face.
- Bradycardia.
- Delayed relaxation of ankle jerk.

Q: What are the **electrocardiographic (ECG)** changes in hypothyroidism?

A: As follows:

- Sinus bradycardia.
- Low-voltage ECG tracing.
- T-wave inversion.

Q: What is the **treatment option**?

A: Lifelong thyroxine replacement, starting with a low dose (25 mcg/d) and then gradually increasing the dose.

N.B. Weight gain, increased sleepiness, cold intolerance and constipation are the usual features of hypothyroidism. Polyserositis may occur in myxoedema. Muscular pain, arthralgia and effusion in any serous cavity may occur. SIADH, high creatinine phosphokinase (CPK), SGPT, SGOT and LDH may also be found.

Case 04: Sick Euthyroid Syndrome

A 65-year-old obese woman was hospitalized with the complaints of fever and cough with purulent sputum for 3 days. Investigations reveal:

- Full blood count: Hb 10.5 g/dL, WBCs 18,540/cmm, polymorphs 82%, lymphocytes 16%, monocytes 2%, platelets 180,000/cmm.
- Chest X-ray: Consolidation (left upper zone).
- ECG: Low-voltage tracing and sinus bradycardia.
- Serum FT₃: 2.2 pmol/L (normal 1.3–3.5 pmol/L).
- Serum FT₄: 104 pmol/L (normal 70–160 pmol/L).
- TSH: 0.2 mIU/L (normal 0.5–5.1 mIU/L).

Q: What is the likely **diagnosis** of thyroid disorder?

A: Sick euthyroid syndrome.

Q: What further **investigation** would you suggest?

A: Repeat FT₃, FT₄ and TSH after cure of pneumonia.

Q: What is the **cause** of ECG abnormality?

A: Obesity.

N.B. In any extrathyroidal illness (acute myocardial infarction, pneumonia, cardiovascular disease [CVD]), there may be abnormal thyroid function tests, although the patient is euthyroid. This is called sick euthyroid syndrome. There may be low total and free T₃ and T₄ along with low or normal TSH. It is confused with secondary hypothyroidism. The tests should be repeated after recovery from the systemic disease, usually after 6 weeks.

Case 05: de Quervain Thyroiditis

A 32-year-old woman presented with fever, dry cough, pain in the throat, headache, body ache, palpitation and intolerance to heat for 1 week. There was fine tremor of the outstretched hands. Palms were warm and sweaty. Thyroid was diffusely enlarged, soft, nontender, but no bruit. Investigations reveal:

- Full blood count: Hb 11.1 g/dL, WBCs 3500/cmm, polymorphs 48%, lymphocytes 52%, ESR 110 mm in the first hour, platelets 365,000/cmm.
- Chest X-ray: Normal.
- Serum FT₃: 8.7 pmol/L (normal 1.3–3.5 pmol/L).
- Serum FT₄: 205 pmol/L (normal 70–160 pmol/L).
- TSH: 0.4 mIU/L (normal 0.5–5.1 mIU/L).
- Radioiodine uptake: After 2 hours, 7% (normal 5%–15%). After 24 hours, 5.1% (normal 15%–30%).

Q: What is the likely **diagnosis**?

A: de Quervain thyroiditis (subacute thyroiditis).

Q: Suggest one **investigation**.

A: Fine-needle aspiration cytology (FNAC) of the thyroid gland.

Q: Mention three other **causes** of such thyroid functions (high T₃ and T₄ but low radioiodine uptake).

A: As follows:

- Postpartum thyroiditis.
- Factitious hyperthyroidism.
- Iodine-induced hyperthyroidism.

N.B. de Quervain thyroiditis is a virus-induced transient inflammation of the thyroid gland, which is usually self-limiting. It is caused by coxsackievirus B4 and also may be associated with influenza, infectious mononucleosis, measles, mumps and common cold. It is more common in females aged 20–40 years. It presents with pain over the thyroid, which radiates to the jaw and ear, and gets worse by coughing, swallowing or movement of the neck. Systemic features are common. Thyroid gland is enlarged and tender. FNAC shows the presence of giant cells. ESR is typically high. Inflammation of thyroid releases thyroid hormones, which are high in the blood, responsible for the features of thyrotoxicosis. This may persist for 4–6 weeks. Iodine uptake is low. Hyperthyroidism followed by transient hypothyroidism may occur. Complete recovery occurs in 4–6 months. Treatment: Symptomatic (nonsteroidal anti-inflammatory drug [NSAID]). Propranolol may be used. Prednisolone 40 mg/d for 3–4 weeks may be needed. Antithyroid drug should not be given.

Case 06: Euthyroid State

A young woman with 4 months' pregnancy presented with the complaints of palpitation, excessive sweating and intolerance to heat. Thyroid gland was diffusely enlarged, nontender and soft. Investigation reveals:

- Full blood count: Hb 10.5 g/dL, WBCs 9800/cmm, polymorphs 66%, lymphocytes 30%, eosinophils 4%, platelets 200,000/cmm, ESR 85 mm in the first hour.
- Serum T₄: 290 nmol/L (normal 70–160 nmol/L).
- Serum T₃: 9 nmol/L (normal 1.32–3.1 nmol/L).
- Serum TSH: 4 mIU/L (normal 1.52–5 mIU/L).

Q: What is your **inference** from the aforementioned result?

A: Euthyroid state.

Q: What further **investigations** should be done?

A: FT_3 and FT_4 .

Q: Mention **four causes** of such thyroid function abnormality.

A: Pregnancy, oral contraceptive pill, oestrogen therapy and acute intermittent porphyria.

N.B. The patient's symptoms are as a result of pregnancy. Thyroid gland may be normally enlarged in pregnancy, so her total T_3 and T_4 are high but TSH is normal.

Any causes of high thyroxine-binding globulin (TBG) will also cause high T_3 and T_4 but FT_3 and FT_4 will be normal. Alternately, any cause of low TBG will also cause low T_3 and T_4 .

Causes of high TBG: Congenital or hereditary, pregnancy, drug (oestrogen, clofibrate, phenothiazine), oral contraceptive pills, acute intermittent porphyria, acute viral hepatitis; also in hypothyroidism.

Causes of low TBG: Hereditary, malnutrition, nephrotic syndrome, liver failure, drugs (sulphonylurea, salicylate, phenytoin, phenylbutazone, anabolic steroid, androgen, corticosteroid), active acromegaly; also in hyperthyroidism.

Case 07: Cushing Syndrome

A housewife aged 40 years presented with frequent headache, vertigo and insomnia for 2 months. Her BP was 160/100 mm Hg. Investigations reveal:

- Full blood count: Hb 11.5 g/dL, WBCs 8300/cmm, polymorphs 64%, lymphocytes 33%, monocytes 3%, ESR 48 mm in the first hour, platelets 270,000/cmm.
- Urine: Glycosuria (+ +), proteinuria (+).
- Serum electrolytes: Sodium 145 mmol/L, chloride 101 mmol/L, potassium 3.1 mmol/L, bicarbonate 30 mmol/L.
- Creatinine: 1.3 mg/dL.
- Chest X-ray: Heart slightly enlarged.
- Fasting blood sugar (FBS): 9.0 mmol/L.

Q: Suggest three **differential diagnoses**.

A: Cushing syndrome, primary aldosteronism and ectopic adrenocorticotrophic hormone (ACTH) syndrome.

Q: What is the **likely diagnosis** in this case?

A: Cushing syndrome.

Q: What **five physical signs** will you see?

A: Obesity, striae, plethoric face, thin skin with bruise, proximal myopathy.

Q: Mention four further investigations.

A: As follows:

- Serum morning and midnight cortisol.
- Dexamethasone suppression test.
- USG of the abdomen (to see the suprarenal gland).
- CT scan or MRI of suprarenal glands.

N.B. Hypertension with hypokalaemia and diabetes mellitus (DM) is highly suggestive of Cushing syndrome. In primary aldosteronism, DM is not common and hypokalaemia is more severe. To diagnose Cushing syndrome, serum morning and midnight cortisol, 24-hour urinary free cortisol and short overnight dexamethasone suppression test should be done to see whether Cushing syndrome is present or not. Then further test should be done to find out causes (e.g., ACTH, X-ray chest, USG of the suprarenal gland, CT or MRI of the suprarenal and pituitary glands).

Case 08: Primary Hyperaldosteronism

A 25-year-old woman had complaints of excessive thirst, weakness, polyuria, nocturia and insomnia for 6 months. Her BP was 165/115 mm Hg. Investigations reveal:

- Full blood count: Hb 12.7 g/dL, WBCs 6800/cmm, polymorphs 60%, lymphocytes 39%, monocytes 1%, ESR 20 mm in the first hour.
- Urea: 38 mg/dL (normal 9–11 mg/dL).
- Creatinine: 1.2 mg/dL (normal 0.68–1.36 mg/dL).
- Serum electrolytes: Sodium 148 mmol/L, chloride 107 mmol/L, potassium 2.8 mmol/L, bicarbonate 32 mmol/L.
- RBS: 9.3 mmol/L.
- Chest X-ray: Cardiomegaly, left ventricular type.

Q: What is your diagnosis?

A: Primary hyperaldosteronism.

Q: Suggest three investigations to confirm your diagnosis.

A: As follows:

- Serum aldosterone and rennin assay.
- 24-hour urine potassium.
- CT scan or MRI of adrenal glands.

N.B. Hypertension with hypokalaemic alkalosis is highly suggestive of primary hyperaldosteronism; it is also called Conn syndrome. It is an aldosterone-secreting tumour responsible for <1% cause of hypertension. Excess aldosterone secretion leads to sodium retention, hypokalaemia and hypertension. It is because of adrenal adenoma in 60% of case (Conn syndrome) and 30% of cases of bilateral adrenal hyperplasia. Serum renin is low in primary aldosteronism, whereas renin is high in secondary aldosteronism. Treatment: If adenoma is present, surgery is needed. If hyperplasia is present, spironolactone 100–400 mg daily is given. For hypertension, amiloride and calcium channel blockers may be used.

Case 09: Hypokalaemic Metabolic Alkalosis

A 45-year-old woman presented with BP of 170/100 mm Hg. Investigation reveals:

- Na^+ : 156 mmol/L.
- K^+ : 2.5 mmol/L.
- Cl^- : 102 mmol/L.
- HCO_3^- : 30 mmol/L.

Q: What are the **abnormalities** in the investigations?

A: As follows:

- Hyponatraemia.
- Hypokalaemia.
- Metabolic alkalosis.

Q: Name three possible **causes** of this investigation finding.

A: As follows:

- Cushing syndrome.
- Conn syndrome (primary hyperaldosteronism).
- Renal artery stenosis.

Q: Name four other **investigations** to confirm the diagnosis.

A: As follows:

- Plasma cortisol.
- Urinary free cortisol.
- Plasma rennin and aldosterone assay (to see the ratio).
- USG of the kidney and the adrenal gland.
- CT or MRI of the suprarenal gland.

Case 10: Addison Disease

A 22-year-old man was admitted with the complaints of weakness and weight loss for several weeks. His BP was 80/50 mm Hg. Investigations reveal:

- Na^+ : 122 mmol/L.
- K^+ : 6.3 mmol/L.
- Cl^- : 98 mmol/L.
- HCO_3^- : 20 mmol/L.

Q: What are the biochemical **abnormalities**?

A: As follows:

- Hyponatraemia.
- Hyperkalaemia.
- Acidosis.

Q: What is the likely **diagnosis**?

A: Addison disease.

Q: Mention one important **clinical sign**.

A: Pigmentation of the skin and the mucous membrane.

Q: What are the common causes?

A: As follows:

- Autoimmune.
- Tuberculosis.

Q: Name other four **investigations** to confirm the diagnosis.

A: As follows:

- Plasma cortisol and ACTH levels.
- Synacthen test.
- USG of the kidney and the suprarenal gland.
- Plain X-ray of the abdomen (to see suprarenal calcification).

***N.B.** In any patient with weakness, hypotension and pigmentation associated with low sodium and high potassium is highly suspected to have Addison disease. It is the primary adrenocortical insufficiency as a result of destruction of the adrenal gland, resulting in deficiency in glucocorticoid and mineralocorticoid. Supine BP may be normal, but a marked drop in systolic pressure on standing may occur. There will be low serum cortisol and high ACTH. Short Synacthen test is helpful for diagnosis. Treatment: Hydrocortisone should be given; mineralocorticoid may be necessary. Steroid card should be maintained.*

Case 11: Diabetic Ketoacidosis (DKA)

A 19-year-old woman was suffering from high-grade fever, productive cough, shortness of breath, diffuse abdominal pain and vomiting. She was emaciated and dehydrated. Investigations reveal:

- Blood glucose: 28 mmol/L.
- Serum electrolytes: Na 118 mmol/L, potassium 4.7 mmol/L, chloride 98 mmol/L and bicarbonate 8.1 mmol/L.
- Serum creatinine: 1.1 mg/dL

Q: What is the likely **diagnosis**?

A: Diabetic ketoacidosis.

Q: What other **investigations** should be done?

A: Urine for ketone bodies.

Q: What are the **complications**?

A: As follows:

- Acute respiratory distress syndrome.
- Thromboembolism.
- DIC.
- ARF.
- Cerebral oedema.

N.B. Dry tongue, weight loss and high blood sugar with severe metabolic acidosis indicate DKA. It is common in type 1 DM. Three main problems in DKA are as follows: (i) hyperglycaemia, (ii) hyperketonaemia and (iii) metabolic acidosis. Marked dehydration is common. Five per cent of cases develop coma in DKA. If bicarbonate is <12 mmol/L, it indicates severe acidosis.

Treatment: IV normal saline rapidly, IV soluble insulin preferably with a pump, potassium therapy, control of infection, correction of acidosis by isotonic 1.26% sodium bicarbonate, if arterial pH is <7 (complete correction of acidosis is avoided because there is a correction of extracellular acidosis, but acidosis in the brain is persistent, which aggravates cellular dysfunction in the brain). Mortality is 5%–10%; higher in the elderly.

Case 12: Hyperosmolar Nonketotic Diabetic Coma with Urinary Tract Infection (UTI)

A 70-year-old woman was suffering from fever and frequency of micturition for 10 days. She was unconscious for the last 2 hours. Her BP was 90/60 mm Hg, pulse 110/min, with marked dehydration. Investigations reveal:

- Full blood count: Hb 11.2 g/dL, WBCs 17,000/cmm, polymorphs 85%, lymphocytes 15%, platelets 210,000/cmm, ESR 12 mm in the first hour.
- Serum electrolytes: Sodium 162 mmol/L, chloride 110 mmol/L, potassium 4.6 mmol/L, bicarbonate 22 mmol/L.
- Serum creatinine: 1.4 mg/dL.
- Urine: Plenty of pus cells, albumin (++), glucose (+++).
- Chest X-ray: Normal.
- CT scan of the brain: Diffuse age-related cerebral atrophy.

Q: What is the likely **diagnosis**?

A: Hyperosmolar nonketotic diabetic coma with UTI.

Q: Suggest two **investigations**.

A: As follows:

- RBS.
- Urine for ketone bodies.

Q: What immediate **therapeutic** measures would you start?

A: As follows:

- IV half-strength saline (0.45%).
- Soluble insulin (preferably with an insulin pump, 2–6 units hourly).
- When osmolality is normal, 0.9% normal saline should be given.
- Other treatment: Nasogastric (NG) tube feeding, catheter insertion if needed, antibiotic administered if infection present, correction of electrolytes, low-dose heparin (as thrombosis is common).

N.B. Hyperosmolar nonketotic diabetic coma (HNDC) may be the first presentation in DM. Common in the elderly, noninsulin-dependent diabetes mellitus (NIDDM), characterized by a very high blood glucose level (>50 mmol/L) and high plasma osmolality. No ketosis results because insulin deficiency is partial and a low level of insulin is present, which is sufficient to prevent ketone body formation but insufficient to control hyperglycaemia. Precipitating factors are a large amount of sweet drinks, infection, steroid, thiazide, myocardial infarction etc. Plasma sodium is usually high. There may be high blood urea nitrogen (BUN); urea, creatinine and serum osmolality may be very high. Mortality rate may be up to 40%.

Case 13: Impaired Glucose Tolerance (IGT)

This is the glucose tolerance test (GTT) report of a 46-year-old woman:

- FBS: 5.1 mmol/L.
- After 0.5 hours: 7.6 mmol/L.
- After 1 hour: 8.3 mmol/L.
- After 1.5 hours: 10.6 mmol/L.
- After 2.0 hours: 10.1 mmol/L.

Q: What is the **glycaemic status**?

A: Impaired glucose tolerance.

Q: What does it **indicate**?

A: The patient is at a high risk of developing type 2 DM.

N.B. When fasting glucose is <7 mmol, but during oral glucose tolerance test (OGTT), blood glucose is 7.8–11.0 mmol/L 2 hours after glucose load, it is called IGT. This patient is at an increased risk of developing frank DM type 2 with time, and macrovascular (cardiovascular) diseases are more common. Lifestyle modification for type 2 DM and annual check-up for glucose are recommended for the patient. Cardiovascular risk factors should be treated aggressively.

Case 14: Renal Glycosuria

A young patient during routine check-up presented with the following laboratory investigation:

- CBC count: Normal.
- Urine R/E: Albumin nil, glucose ++, few epithelial cells, RBCs nil, pus cells nil.
- Blood glucose: 5.5 mmol/L.

Q: What is the **diagnosis**?

A: Renal glycosuria.

Q: What is the **prognosis**?

A: It is a benign disease.

N.B. Renal glycosuria results from low renal threshold for glucose. Blood glucose level is normal. It is the most common cause of glycosuria and often found in pregnancy and young individuals. It is usually asymptomatic and rarely may lead to polyuria and polydipsia.

X-RAY, CT
AND MRI

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'Treat the patient, not the X-ray'
—James M. Hunter

PLEURAL EFFUSION

Fig. A: Left-sided pleural effusion.

Q: Write down the radiological **findings** of the X-ray shown in Figure A.

A: X-ray chest posteroanterior (PA) view showing:

- Dense homogeneous opacity in the left lower zone with a curvilinear upper border.
- There is obliteration of the left costophrenic angle.
- Trachea and heart (mediastinum) are shifted to the right.

Q: What is your radiological **diagnosis**?

A: Left-sided pleural effusion.

Q: Write down **one percussion** and **two auscultatory findings** of the chest.

A: As follows:

- Percussion note stony dull.
- On auscultation: Diminished or absent breath sound and diminished or absent vocal resonance.

Q: Write down four common **causes**.

A: As follows:

- Pulmonary tuberculosis (TB).
- Parapneumonia.
- Bronchial carcinoma.
- Pulmonary infarction.

Q: Write down other **investigations** to confirm the diagnosis.

A: As follows:

- Complete blood cell (CBC) count with erythrocyte sedimentation rate (ESR).
- Tuberculin test.
- Pleural fluid analysis (physical character, cytology, biochemistry, Gram [Gm] stain, culture, acid-fast bacilli [AFB], malignant cell, adenosine deaminase [ADA]).
- Pleural biopsy.
- Bronchoscopy and biopsy (if needed in bronchial carcinoma).

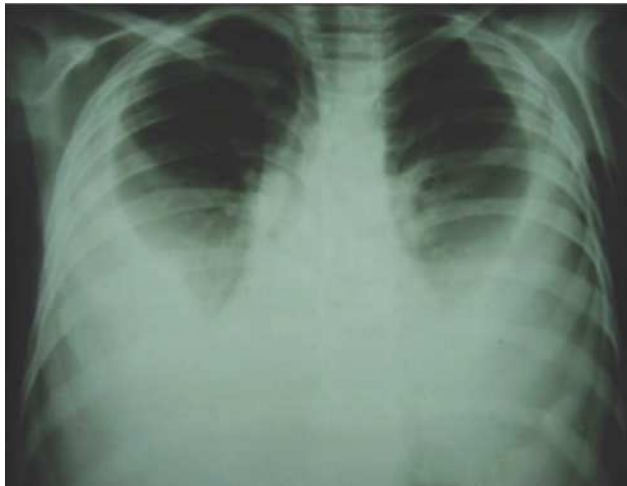


Fig. B: Bilateral pleural effusion.

Q: Write down the radiological **findings** of the X-ray shown in Figure B.

A: X-ray chest PA view showing dense homogeneous opacity with a curvilinear upper border in both lower zones obliterating both costophrenic angles.

Q: What is your radiological **diagnosis**?

A: Bilateral pleural effusion.

Q: What are the **causes**?

A: As follows:

- Cirrhosis of liver.
- Nephrotic syndrome.
- Congestive cardiac failure.
- Bilateral extensive TB.
- Collagen disease: Systemic lupus erythematosus (SLE), rheumatoid arthritis (RA).

Q: Write down the radiological **findings** of the X-ray shown in Figure C.

A: X-ray chest right decubitus view showing dense homogeneous opacity in the peripheral part of the chest with a clear upper border.

Q: What is your radiological **diagnosis**?

A: Right-sided pleural effusion.



Fig. C: Right-sided pleural effusion (decubitus view).

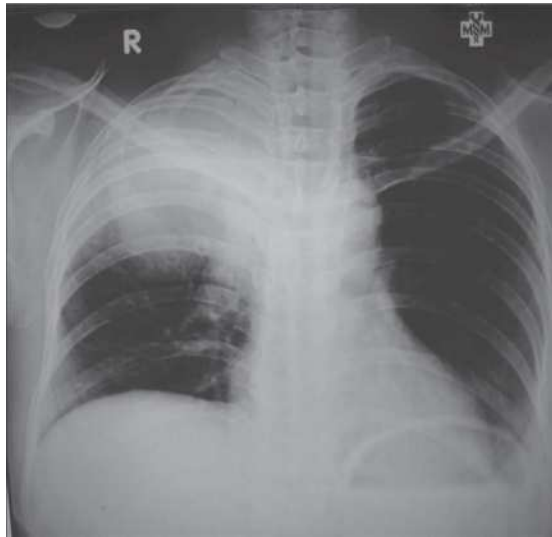
MASS LESION

Fig. A: Mass lesion (bronchial carcinoma) in the right lung.

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing opacity with an irregular margin, occupying the right upper and part of the middle zone.

Q: What is your radiological **diagnosis**?

A: Bronchial carcinoma.

Q: Mention two **differential** diagnoses.

A: As follows:

- TB.
- Consolidation.

Q: Mention three **investigations** to confirm your diagnosis?

A: As follows:

- Sputum for malignant cells (exfoliative cytology).
- Computed tomography (CT)- or ultrasonography-guided fine-needle aspiration cytology (FNAC).
- Bronchoscopy and biopsy.
- If palpable lymph node, then FNAC or biopsy.

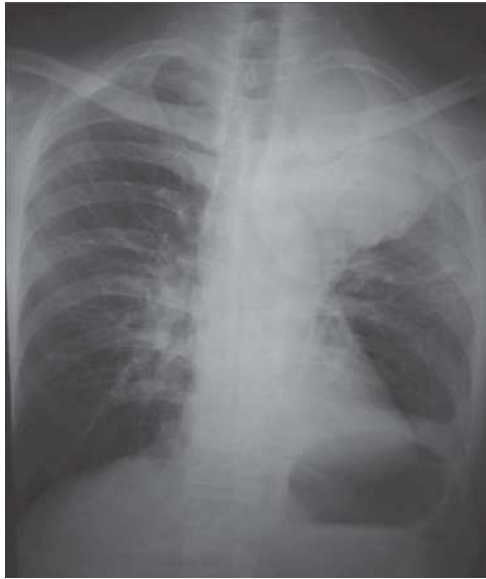


Fig. B: Bronchial carcinoma with left phrenic nerve palsy.

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

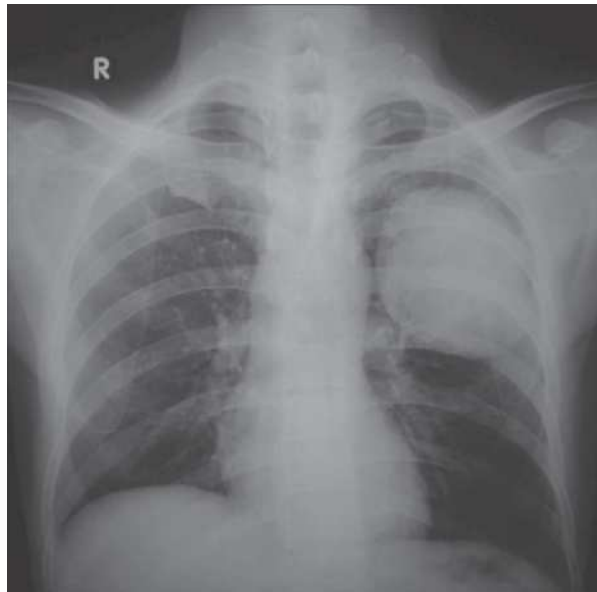
A: X-ray chest PA view showing:

- Opacity with irregular margin in the left upper and part of the middle zone.
- Left dome of the diaphragm is raised.

Q: What is your radiological **diagnosis**?

A: Bronchial carcinoma with left phrenic nerve palsy.

SOLITARY PULMONARY NODULE



Left-sided solitary pulmonary nodule.

Q: Write down the radiological **finding** of this X-ray.

A: Chest X-ray (CXR) PA view showing a homogeneous, rounded, nodular shadow with a clear margin in the left middle zone.

Q: Mention five **causes**.

A: As follows:

- Consolidation.
- Tuberculoma.
- Bronchial carcinoma.
- Secondary deposit.
- Bronchial adenoma.
- Lung abscess before burst.
- Hydatid cyst.

N.B. Others causes are encysted pleural effusion, hamartoma, rheumatoid nodule, Wegener granulomatosis, aspergilloma, neurofibroma, fungal infection or granuloma (histoplasmosis).

Q: Mention one **investigation** to confirm the diagnosis.

A: CT-guided FNAC.

Q: What **investigations** should be done?

A: As follows:

- CXR lateral view.
- CBC count and ESR.
- Sputum for Gm staining, culture and sensitivity (C/S), AFB, malignant cells.
- Mantoux test (MT).
- CT-guided FNAC.
- Bronchoscopy and bronchial brushing for AFB, malignant cells.

Q: How would you **differentiate** neurofibroma from dermoid cyst radiologically?

A: By lateral film:

- If neurofibroma: It is in the posterior mediastinum.
- If dermoid cyst: It is in the anterior mediastinum.

MULTIPLE SECONDARIES IN LUNG

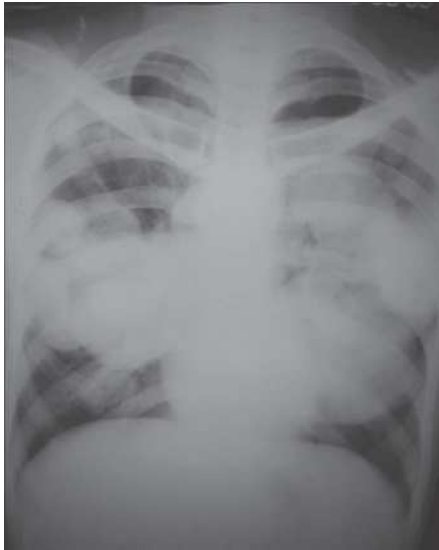


Fig. A: Multiple secondaries in both lungs.

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing multiple, nodular shadows of variable sizes and shapes, some having 'cannon-ball' appearance in both lung fields.

Q: What is your radiological **diagnosis**?

A: Multiple secondary deposits in the lung.

Q: Mention five **sources** of such lesion.

A: As follows:

- Carcinoma of the stomach.
- Carcinoma of the prostate.
- Carcinoma of the breast.
- Teratoma.
- Renal cell carcinoma.
- Carcinoma of the thyroid gland.

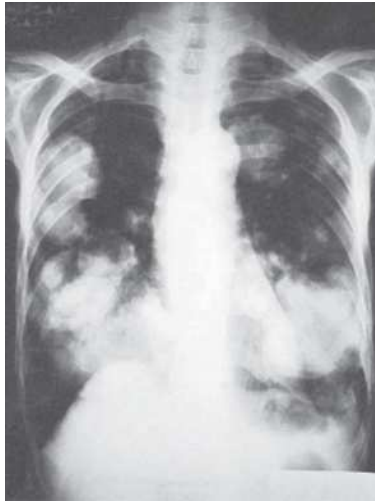


Fig. B: Multiple secondaries in both lungs.

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

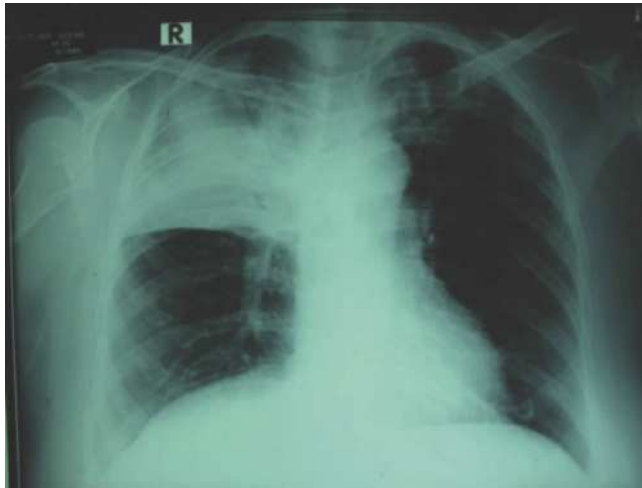
A: X-ray of chest PA view showing:

- Multiple, nodular shadows of variable sizes and shapes, some having 'cannon-ball' appearance in both lung fields.
- Right dome of the diaphragm is elevated.

Q: What is your radiological **diagnosis**?

A: Multiple secondary deposits in the lung with right phrenic nerve palsy.

CONSOLIDATION



Right-sided consolidation.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing dense, homogeneous opacity involving the right upper and part of the middle zone with air bronchogram within it.

Q: What are the differential **diagnoses** from this X-ray?

A: As follows:

- Consolidation.
- Bronchial carcinoma.
- TB.

Q: What is the **likely diagnosis**?

A: Consolidation.

Q: Write down the **percussion and auscultation findings** of this patient.

A: As follows:

- Percussion note is dull (or woody dull).
- Auscultation: Bronchial breath sound, increased vocal resonance.

Q: Write down other **investigations** to confirm the diagnosis.

A: As follows:

- CBC count with ESR.
- Sputum for Gm staining, C/S.
- Sputum for AFB and malignant cells.

Q: Mention two **complications**?

A: As follows:

- Lung abscess.
- Empyema.

Q: What is the commonest **organism**?

A: Pneumococci.

LUNG ABSCESS

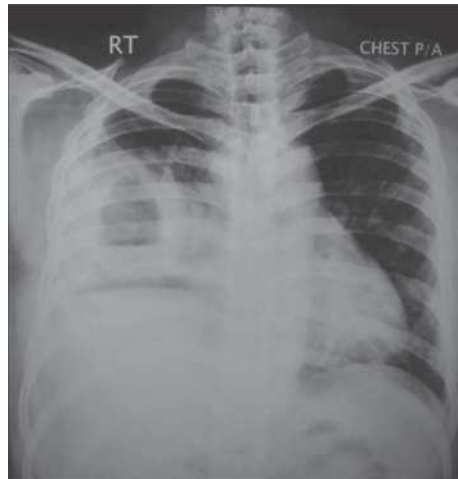


Fig. A: Right-sided lung abscess.

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing a cavity with air–fluid level in the right middle and lower zones.

Q: What is your **diagnosis**?

A: Right-sided lung abscess.

Q: Write down the **percussion and auscultation findings** of this patient.

A: As follows:

- Percussion note is dull (may be dull in the lower part and hyper-resonant in the upper part).
- Auscultation: Bronchial breath sound, increased vocal resonance.

Q: What other **investigations** will you do to confirm this diagnosis?

A: As follows:

- CBC count with ESR.
- CT scan of the chest.
- Sputum for Gm staining, C/S and AFB.

Q: Write down three important **complications**.

A: As follows:

- Empyema thoracis.
- Bronchiectasis.
- Cerebral abscess.

Q: What is the **commonest cause**?

A: Aspiration of an infected material as a result of any cause.

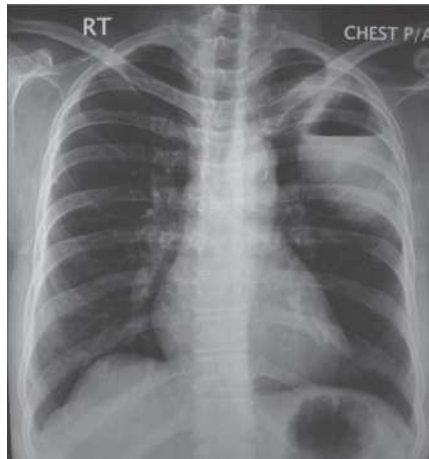


Fig. B: Left-sided lung abscess.

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest PA view showing a cavity with air–fluid level in the left upper and part of the middle zone.

Q: What is your **diagnosis**?

A: Left-sided lung abscess.

PULMONARY TUBERCULOSIS

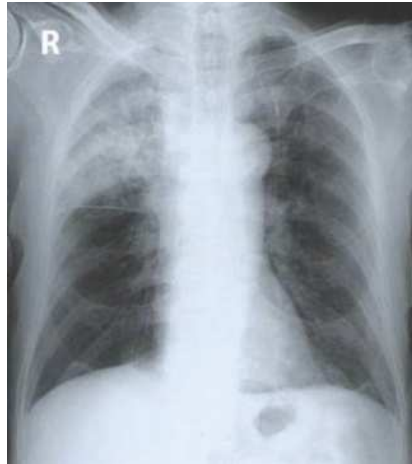


Fig. A: Right-sided pulmonary TB.

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing patchy opacities with some translucent shadows within it involving the right upper and part of the middle zone.

Q: What is the radiological **diagnosis**?

A: Right-sided pulmonary TB.

Q: Write down other **investigations** to confirm the diagnosis.

A: As follows:

- CBC count with ESR.
- Sputum for AFB staining (three consecutive samples).
- Tuberculin test.
- PCR for TB.

Q: How to **treat**?

A: Standard anti-TB therapy for 6 months in the following regimen:

- Initial phase (2 months): Isoniazid (INH) + rifampicin + pyrazinamide + ethambutol.
- Continuation phase (4 months): INH + rifampicin.
- Tab. pyridoxine (20 mg) for 6 months.

Q: Mention one **complication** of each drug.

A: As follows:

- Rifampicin: Hepatitis.
- INH: Peripheral neuropathy.
- Ethambutol: Optic neuritis.
- Pyrazinamide: Hepatitis (also hyperuricaemia and gout).



Fig. B: Bilateral extensive TB.

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest PA view showing patchy opacities involving both the upper and middle zones in both right and left lungs.

Q: What is the radiological **diagnosis**?

A: Bilateral extensive TB.



Fig. C: Tubercular cavity in the left side.

Q: Write down the radiological **finding** of the X-ray shown in Figure C.

A: X-ray chest PA view showing patchy opacities with a cavity in the left upper zone.

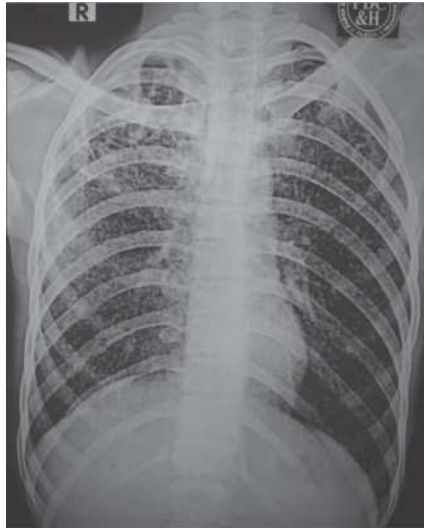
Q: What is the radiological **diagnosis**?

A: Pulmonary TB.

Q: What is the **significance** of this finding?

A: Presence of the cavity indicates an active and open case of TB.

MILIARY TUBERCULOSIS



Miliary TB.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing multiple miliary mottling involving all the zones of both lung fields.

Q: What is the **diagnosis**?

A: Miliary TB.

Q: Mention four common **differential** diagnoses.

A: As follows:

- Sarcoidosis.
- Pulmonary eosinophilia.
- Histoplasmosis.
- Pneumoconiosis.

Q: Mention four **investigations**.

A: As follows:

- CBC count with ESR and circulating eosinophil count.
- Sputum for AFB.
- Tuberculin test.
- Bronchoscopy and bronchoalveolar lavage.

Q: What are the common **presentations** of this patient?

A: Low-grade continued fever, mostly evening rise, night sweat, weight loss, cough with haemoptysis etc.

CALCIFICATION OF THE LUNG PARENCHYMA



Calcification of lung parenchyma.

Q: Write down the radiological **findings** in this X-ray.

A: X-ray chest PA view showing multiple calcified shadows of variable sizes and shapes, involving all the zones of both lung fields.

Q: What is your radiological **diagnosis**?

A: Multiple calcifications in the lung parenchyma.

Q: Mention five **causes**.

A: As follows:

- TB (usually healed, commonly in the upper zone).
- Adult chickenpox pneumonia (widely distributed, usually small, 1–3 mm).
- Histoplasmosis (surrounded by a small halo) and other fungal infection.
- Hamartoma (popcorn calcification).
- Hypercalcaemia as a result of any cause.
- Alveolar microlithiasis.
- Silicosis.

EMPHYSEMA



Emphysema.

Q: Write down the radiological **finding** of this X-ray.

A: CXR PA view showing:

- Lung fields are hypertranslucent.
- Low and flat diaphragm.
- Heart is elongated and tubular.
- Ribs are widely spaced.

Q: What is your radiological **diagnosis**?

A: Pulmonary emphysema.

Q: What is the **pathognomonic sign** in the CXR of this disease?

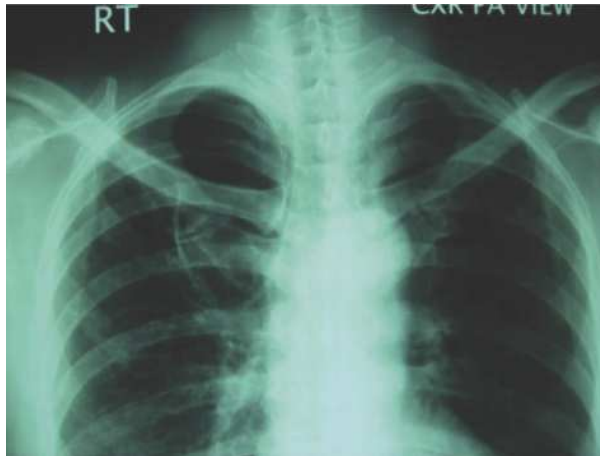
A: Bullae.

Q: Mention two **investigations**.

A: As follows:

- Lung function tests (obstructive type: Forced expiratory volume in 1 second [FEV₁] and forced vital capacity [FVC] are reduced and the ratio of FEV₁:FVC is also reduced).
- High-resolution computed tomography (HRCT) of the chest.

BULLAE



Bullae.

Q: Write down the radiological **findings** in this X-ray.

A: X-ray chest PA view showing a large translucent area in the right upper zone with no lung marking and blood vessel, bounded by a thin-line (hairline) shadow.

Q: What is your radiological **diagnosis**?

A: Right-sided giant bullae.

Q: What are the **other possibilities**?

A: As follows:

- Apical pneumothorax (collapsed lung margin should be present in such a case).
- Big cavity.

Q: Mention three **complications**.

A: As follows:

- Rupture causing pneumothorax.
- Secondary infection.
- Aspergilloma.

SURGICAL EMPHYSEMA



Surgical emphysema with a bilateral chest tube.

Q: Write down the radiological **findings** in this X-ray.

A: X-ray chest PA view showing:

- Increased translucency with collapsed lung margin on the right side.
- There are multiple translucent shadows in the soft tissue outside the thoracic cavity on both sides.
- Intrathoracic (IT) tube is seen on both sides.

Q: What is your radiological **diagnosis**?

A: Right-sided pneumothorax with subcutaneous emphysema.

Q: Mention three **causes**.

A: As follows:

- Traumatic (road traffic accident, penetrating injury).
- During aspiration of pneumothorax or introduction of the IT tube.
- Acute severe asthma (as a result of rupture of alveoli).
- Intermittent positive pressure ventilation.

PNEUMOTHORAX

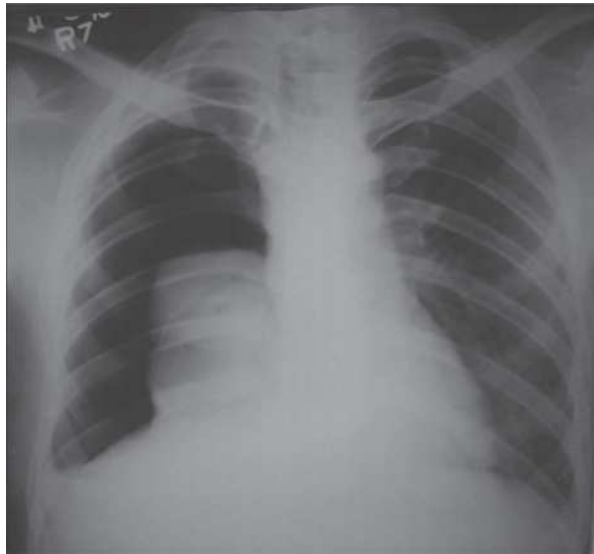


Fig. A: Right-sided pneumothorax.

Q: Write down the radiological **findings** of the X-ray shown in Figure A.

A: X-ray chest PA view showing a hypertranslucent area without bronchovascular markings with collapsed lung margin on the right side.

Q: What is the radiological **diagnosis**?

A: Right-sided pneumothorax.

Q: What is the **type**?

A: Closed.

Q: Write down the **findings** in percussion and auscultation.

A: As follows:

- Percussion note is hyper-resonant on the left side.
- On auscultation: Diminished (or absent) breath sound and diminished (or absent) vocal resonance on the left side.

Q: Write down three common **causes**.

A: As follows:

- Rupture of subpleural emphysematous bullae.
- Rupture of subpleural tuberculous focus.
- Rupture of subpleural bleb in young patients.

Q: Write down the **principle of management** of this patient.

A: As follows:

- If small and asymptomatic: Complete rest and follow-up.
- If large: Intercostal chest tube drainage (or water seal drainage).
- Treatment of the underlying cause.

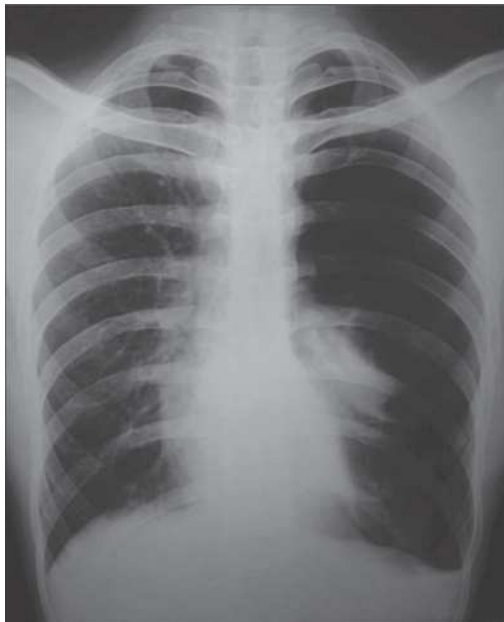


Fig. B: Left-sided pneumothorax.

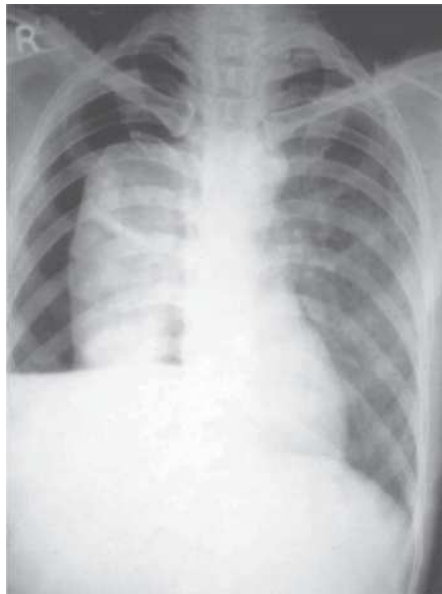
Q: Write down the radiological **findings** of the X-ray shown in Figure B.

A: X-ray chest PA view showing a hypertranslucent area without bronchovascular markings with collapsed lung margin on the left side.

Q: What is the radiological **diagnosis**?

A: Left-sided pneumothorax.

HYDROPNEUMOTHORAX



Right-sided hydropneumothorax.

Q: Write down the radiological findings of this X-ray.

A: X-ray chest PA view showing:

- Increased translucency with collapsed lung margin on the right side.
- There is a horizontal fluid level with obliteration of right costophrenic and cardiophrenic angles.

Q: What is your radiological diagnosis?

A: Right-sided hydropneumothorax.

Q: Mention one important bedside physical finding.

A: Succussion splash.

Q: What are the causes?

A: As follows:

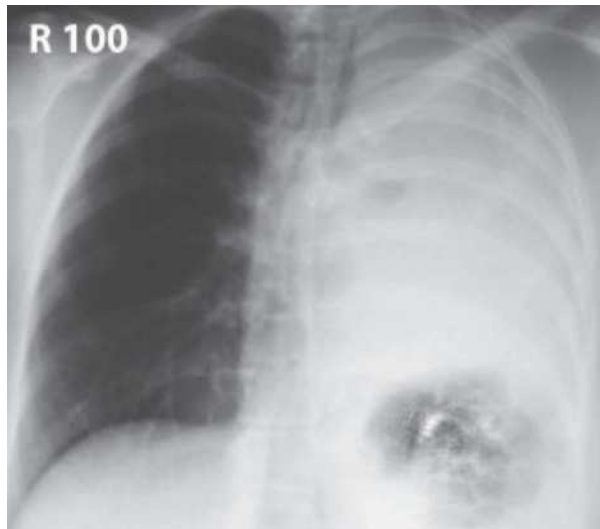
- Iatrogenic (during aspiration of pleural fluid)—common cause.
- Bronchopleural fistula.
- Trauma (penetrating injury, thoracic surgery).
- Rupture of lung abscess.
- Oesophageal rupture.
- Erosion by bronchial carcinoma.
- Pulmonary TB.

Q: How to treat?

A: As follows:

- Insertion of the IT tube.
- Treatment of the specific cause.

COLLAPSE OF LUNG



Collapse of the left lung.

Q: What is your radiological finding?

A: X-ray chest PA view showing:

- Homogeneous opacity involving the whole left lung field.
- Trachea and heart shifted to the left.
- Hypertranslucency of the right lung field.

Q: What is your radiological diagnosis?

A: Collapse of the left lung.

Q: Mention two causes.

A: As follows:

- Bronchial carcinoma with complete bronchial obstruction.
- Foreign body in the left bronchus.

Q: Mention three physical findings.

A: As follows:

- Palpation: Trachea and apex beat shifted to the left.
- Percussion: Dullness in the whole left hemithorax.
- Auscultation: Breath sound and vocal resonance are diminished on the left side.

Q: Mention two further investigations.

A: As follows:

- CT scan of the chest.
- Bronchoscopy.

RIB RESECTION



Rib resection.

Q: Write down the radiological findings in this X-ray.

A: X-ray chest PA view showing:

- There is rib resection on the left side.
- Homogeneous opacity with air–fluid level involving the left lower and part of the middle zone. The rest of the left lung field shows hypertranslucency.
- Left costophrenic and cardiophrenic angles are obscure.
- Trachea and heart are shifted to the left.
- The right lung field shows compensatory hypertranslucency.

Q: What is your radiological diagnosis?

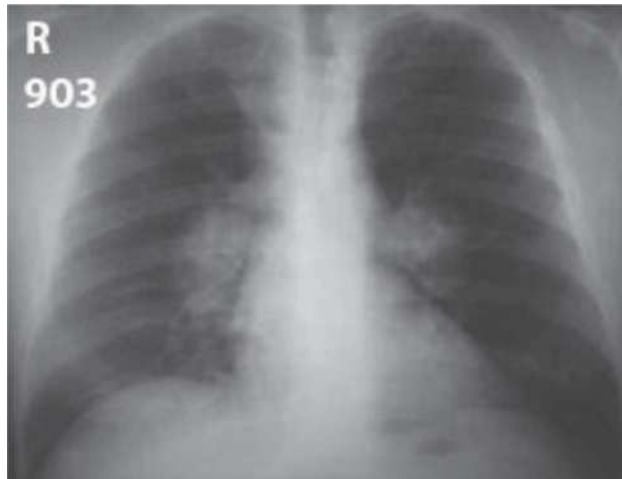
A: Pneumonectomy of the left lung.

Q: Mention five indications.

A: As follows:

- Bronchial carcinoma (if localized).
- Bronchial adenoma.
- Extensive bronchiectasis.
- Extensive fibrosis with repeated chest infection.
- In some cases of TB (multidrug-resistant TB [MDR-TB] or no response to the drug).

BILATERAL HILAR LYMPHADENOPATHY



Bilateral hilar lymphadenopathy.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing bilateral hilar lymphadenopathy.

Q: Write three **causes**.

A: As follows:

- Sarcoidosis.
- Lymphoma.
- TB.

Q: Mention one **drug** that can cause this type of finding.

A: Anticonvulsant such as phenytoin or diphenylhydantoin (called pseudolymphoma).

Q: Mention three **physical findings**.

A: As follows:

- Lymphadenopathy in other parts of the body.
- Hepatomegaly.
- Splenomegaly.

Q: Write two **investigations**.

A: As follows:

- CBC count, ESR.
- Tuberculin test.
- FNAC or biopsy of the lymph node.

SARCOIDOSIS



Bilateral hilar lymphadenopathy with parenchymal lung involvement.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing:

- Bilateral hilar lymphadenopathy.
- Reticulonodular shadow in both lung fields.

Q: What is your radiological **diagnosis**?

A: Sarcoidosis.

Q: Mention four **physical findings**.

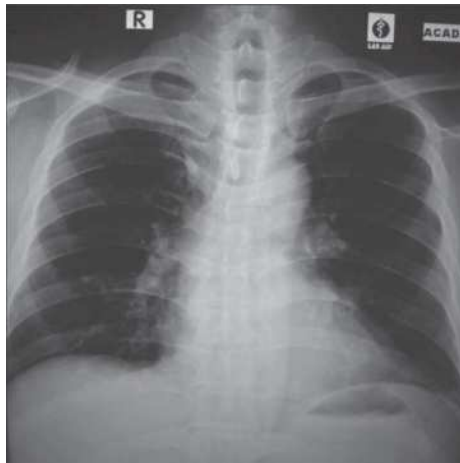
A: As follows:

- Erythema nodosum.
- Lymphadenopathy in other parts of the body.
- Hepatosplenomegaly.
- Bilateral parotid enlargement.

Q: Write three **investigations** to confirm.

A: As follows:

- Tuberculin test (usually zero).
- FNAC or biopsy from the lymph node.
- Bronchoscopy and biopsy.

AZYGOS LOBE

Azygos lobe.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing an inverted comma-shaped opacity in the right apical region.

Q: What is your radiological **diagnosis**?

A: Azygos lobe.

Q: What is its **significance**?

A: It is physiological and may be confused with pathological conditions such as consolidation, TB and mass lesion.

CAVITY SUPERIMPOSED ON CARDIAC SHADOW



Cavity superimposed on the cardiac shadow.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing air–fluid level superimposed on the cardiac shadow.

Q: Mention three **differential** diagnoses.

A: As follows:

- Hiatus hernia.
- Achalasia cardia.
- Lung abscess.

Q: Mention three **investigations**.

A: As follows:

- CXR left lateral view.
- Barium swallow of the oesophagus in Trendelenburg position.
- Endoscopy.

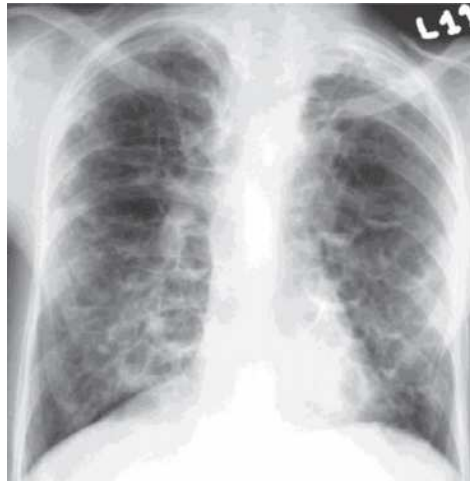
BRONCHIECTASIS

Fig. A: Bilateral bronchiectasis.

Q: Write down the radiological **findings** of the X-ray shown in Figure A.

A: X-ray chest PA view showing multiple ring shadows involving the middle and lower zones of both lung fields, more on the right side.

Q: What is your radiological **diagnosis**?

A: Bilateral bronchiectasis

Q: What is the **likely cause** in this disease?

A: Cystic fibrosis.

Q: Write down **one investigation** to confirm the diagnosis.

A: HRCT of the chest.

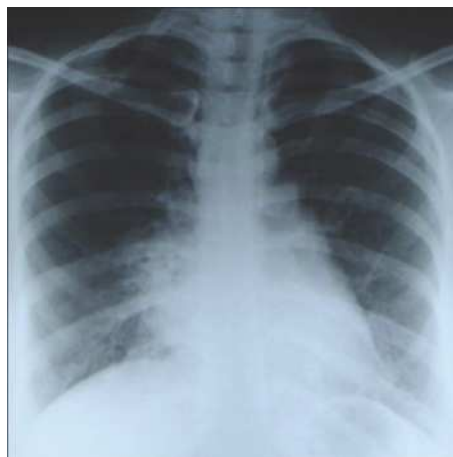


Fig. B: Right-sided bronchiectasis.

Q: Write down the radiological **findings** of the X-ray shown in Figure B.

A: X-ray chest PA view showing multiple ring shadows involving the lower zone of the right lung field.

Q: What is your radiological **diagnosis**?

A: Right-sided bronchiectasis.

Q: What is the **commonest cause**?

A: Childhood pneumonia or pulmonary infection after whooping cough and measles.

Q: What is the **definitive treatment** of this case?

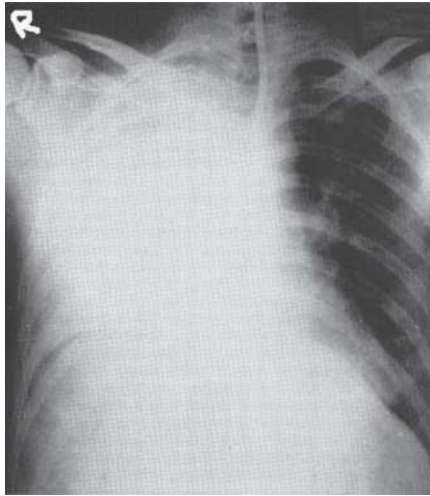
A: Lobectomy.

Q: Mention three other **treatment** modalities.

A: As follows:

- Postural drainage.
- Chest physiotherapy.
- Antibiotics, if infection is present.

HOMOGENEOUS OPACITY OF ONE HEMITHORAX



Homogeneous opacity of the right lung.

Q: Write down the radiological **findings** of this X-ray.

A: X-ray chest PA view showing homogeneous opacity involving the whole right hemithorax.

Q: Mention three **differential diagnoses**.

A: As follows:

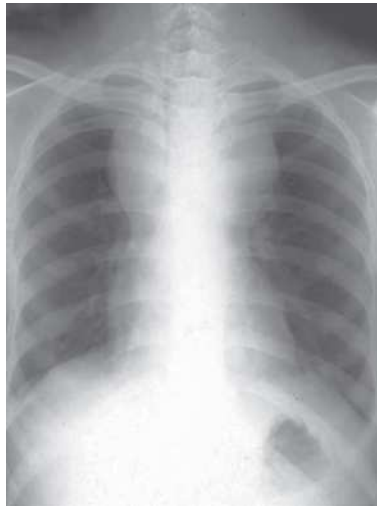
- Massive consolidation.
- Massive pleural effusion.
- Complete collapse of the right lung.

Q: Mention three **investigations**.

A: As follows:

- CT scan of the chest.
- Bronchoscopy and biopsy.
- CT-guided FNAC.

MEDIASTINAL WIDENING



Mediastinal widening.

Q: Write down the radiological **findings** of this X-ray.

A: X-ray chest PA view showing widening of the superior mediastinum.

Q: Mention four differential **diagnoses**.

A: As follows:

- Lymphoma.
- Sarcoidosis.
- Bronchial carcinoma.
- Retrosternal goitre.

Q: Mention one important **physical finding** of this patient.

A: Puffiness of the face with engorged, nonpulsatile neck veins as a result of superior vena caval obstruction.

Q: Mention four other **investigations**.

A: As follows:

- CBC count.
- X-ray chest lateral view.
- CT scan of the chest.
- CT-guided FNAC.

GAS UNDER THE DIAPHRAGM

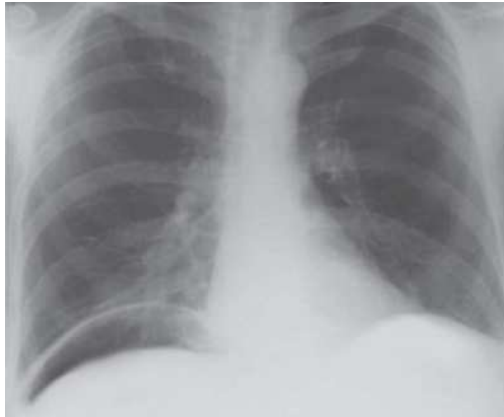


Fig. A: Gas under the right dome of the diaphragm.

Q: Write down the radiological **findings** of the X-ray shown in Figure A.

A: X-ray chest PA view showing gas under the right dome of the diaphragm.

Q: What is your radiological **diagnosis**?

A: Perforation of gas containing the hollow viscus.

Q: Write down two common **causes**.

A: As follows:

- Perforation of chronic duodenal ulcer.
- Perforation of the ileum (as a result of typhoid, TB, Crohn disease).

Q: Mention one most important **clinical finding**.

A: Obliteration of liver dullness on percussion.

Q: Write down the modalities of treatment.

A: As follows:

- Nothing by mouth.
- Nasogastric suction.
- Intravenous (IV) fluid.
- Broad-spectrum antibiotic with metronidazole.
- Surgical repair.

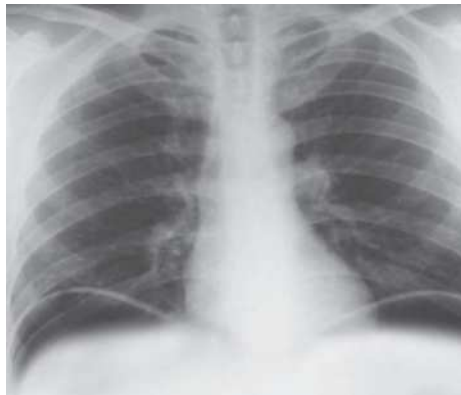


Fig. B: Gas under both domes of the diaphragm.

Q: Write down the radiological **findings** of the X-ray shown in Figure B.

A: X-ray chest PA view showing gas under both domes of the diaphragm.

Q: Write down five **causes**.

A: As follows:

- Perforation of the hollow viscus containing gas.
- Laparotomy or laparoscopy.
- Penetrating injury of the abdomen.
- Burst appendicitis.
- Tubal insufflation.

SITUS INVERSUS



Situs inversus.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing:

- Cardiac apex directed towards the right side.
- Fundic gas shadow is on the right side.
- Left dome of the diaphragm is raised.

Q: What is your radiological **diagnosis**?

A: Situs inversus.

Q: What is the **prognosis**?

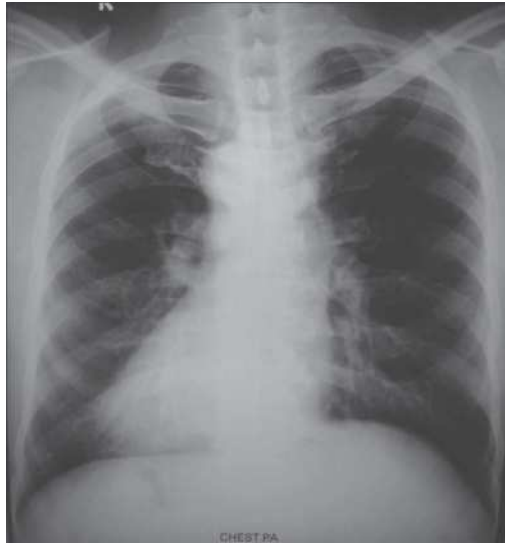
A: Normal life span.

Q: What is the clinical **importance** of this disorder?

A: As follows:

- The patient's appendix is on the left side. So, the appendicitis may be missed, as it is on the left side.
- Sometimes, liver biopsy is done mistakenly on the right side; it will be missed.

DEXTROCARDIA



Dextrocardia.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing:

- Cardiac apex directed towards the right side.
- Fundic gas shadow is on the left side.

Q: What is your radiological **diagnosis**?

A: Dextrocardia.

Q: What other **investigation** should be done? Why?

A: X-ray of paranasal sinuses (PNS) to see sinusitis or frontal sinus agenesis, which may be present in Kartagener syndrome.

N.B. Kartagener syndrome is characterized by dextrocardia, bronchiectasis and frontal sinus agenesis or sinusitis.

MITRAL STENOSIS



Fig. A: Mitral stenosis.

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing fullness of the pulmonary conus with straightening of the left border of the heart.

Q: What is your radiological **diagnosis**?

A: Mitral stenosis.

Q: Mention four important radiological **findings that may be present** in this disease.

A: As follows:

- Widening of the carina with horizontal left main bronchus.
- Double contour of the right border of the heart.
- Upper lobe diversion.
- Kerley B line.

Q: Mention one **investigation** to confirm your diagnosis.

A: Colour Doppler echocardiography.

Q: Mention two **complications**.

A: As follows:

- Congestive cardiac failure (CCF).
- Atrial fibrillation.



Fig. B: Mitral stenosis with mitral regurgitation.

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest PA view showing:

- Straightening of the left cardiac border.
- Heart is enlarged in the transverse diameter.

Q: What is your radiological **diagnosis**?

A: Mitral stenosis with mitral regurgitation.

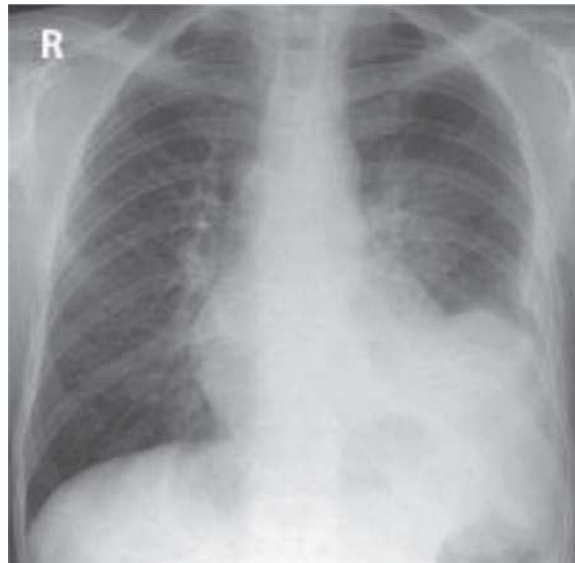
Q: What is the **predominant** lesion?

A: Mitral regurgitation (as the heart is enlarged).

Q: Mention one **investigation** to confirm your diagnosis.

A: Colour Doppler echocardiography.

VENTRICULAR ANEURYSM



Ventricular aneurysm.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing:

- Heart is enlarged in the transverse diameter.
- There is bulging of the left lower border with calcification of the outer border.

Q: What is your radiological **diagnosis**?

A: Ventricular aneurysm.

Q: Mention one investigation to **confirm** your diagnosis.

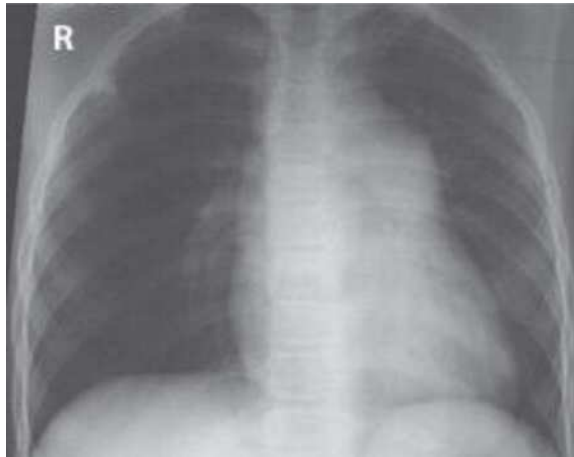
A: Echocardiography.

Q: Mention three **complications**.

A: As follows:

- Acute left ventricular failure (LVF).
- Arrhythmia.
- Systemic embolism.

ATRIAL SEPTAL DEFECT (ASD)



Atrial septal defect.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing:

- Heart is enlarged in the transverse diameter.
- There is fullness of the pulmonary conus with bulging of the left border.

Q: What is your radiological **diagnosis**?

A: Atrial septal defect.

Q: Mention one investigation to **confirm** your diagnosis.

A: Colour Doppler echocardiography.

Q: Mention three **auscultatory findings**.

A: As follows:

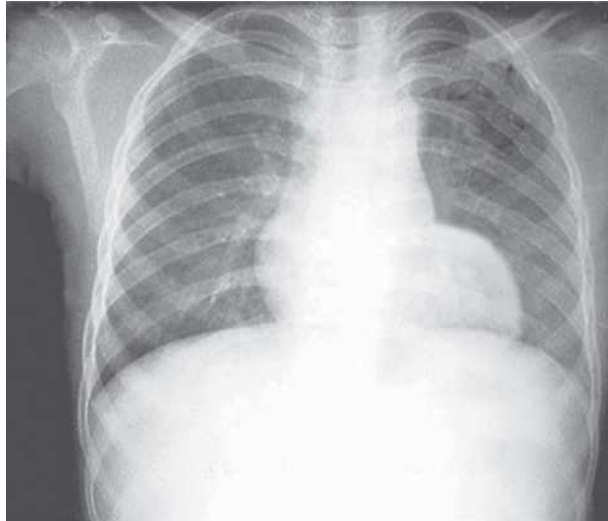
- Wide, fixed splitting of the second heart sound.
- Mid-diastolic murmur.
- Ejection systolic murmur.

Q: Mention the **ECG finding**.

A: As follows:

- In ostium primum defect: Right bundle-branch block (RBBB) with left-axis deviation.
- In ostium secundum defect: RBBB with right-axis deviation.

TETRALOGY OF FALLOT



Tetralogy of Fallot.

Q: Write down the radiological **finding** of this X-ray.

A: CXR PA view showing:

- Boot-shaped heart (apex is lifted up and there is a concavity or bay in the region of the pulmonary artery).
- Oligemic lung fields.

Q: What is your radiological **diagnosis**?

A: Tetralogy of Fallot (TOF).

Q: Mention the **anatomical defects** in this disease.

A: As follows:

- Pulmonary stenosis (valvular or infundibular).
- Overriding and dextroposition of the aorta (aortic origin two-thirds from the left ventricle and one-third from the right ventricle).
- Right ventricular hypertrophy.
- Ventricular septal defect (VSD) (large subaortic).

Q: What are the **physical findings**?

A: As follows:

- Clubbing and central cyanosis.
- Palpation: Left parasternal lift, epigastric pulsation and systolic thrill in the pulmonary area.
- Auscultation: First heart sound is normal, P2 is soft or absent in the pulmonary area, A2 is normal. Harsh ejection systolic murmur in the pulmonary area radiating to the suprasternal notch.

Q: What are the **complications**?

A: As follows:

- Infective endocarditis.
- Paradoxical emboli.
- Cerebral abscess (in 10% of cases).
- Polycythaemia secondary to hypoxia (it may cause cerebral infarction).

Q: Mention two **investigations**.

A: As follows:

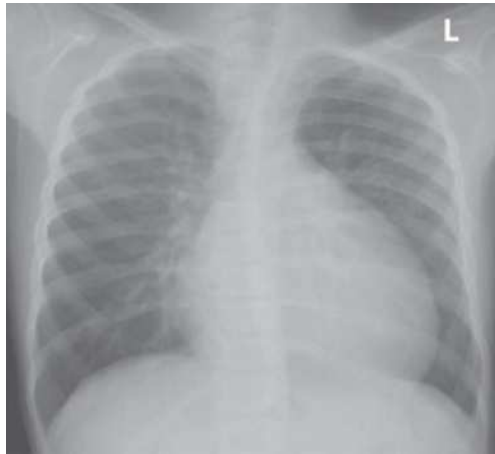
- Colour Doppler echocardiography.
- Cardiac catheterization.

Q: How to **treat**?

A: As follows:

- Surgical correction should be done.
- If total correction is not possible, then temporarily Blalock–Taussig shunt is performed. Corrective surgery is done later on.
- Prophylactic antibiotic to prevent infective endocarditis.

CARDIOMEGALY



Cardiomegaly.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray chest PA view showing the increased transverse diameter of the cardiac shadow.

Q: What is the radiological **diagnosis**?

A: Cardiomegaly.

Q: Mention five important common **causes** of producing this X-ray finding.

A: As follows:

- Pericardial effusion.
- Multiple valvular heart disease.
- Biventricular failure.
- Myocarditis.
- Cardiomyopathy.
- Shunt anomaly (VSD, ASD, patent ductus artery [PDA]).
- Hyperdynamic circulation as a result of any cause (anaemia, beriberi, thyrotoxicosis, arteriovenous fistula etc.).

Q: What other **investigations** should be done?

A: As follows:

- ECG.
- Echocardiography.

PERICARDIAL EFFUSION



Pericardial effusion.

Q: Write down the radiological **findings** of this X-ray.

A: X-ray chest PA view showing:

- Heart is enlarged in the transverse diameter, globular, pear-shaped with a clear margin.
- Lung fields are oligoemic.

Q: What is the radiological **diagnosis**?

A: Pericardial effusion.

Q: Name five common **causes** of pericardial effusion.

A: As follows:

- TB.
- Lymphoma.
- Following acute pericarditis.
- Collagen diseases.
- Myxoedema.

Q: Write down four important **signs** in the favour of your diagnosis.

A: As follows:

- Raised jugular venous pressure (JVP).
- Narrow pulse pressure; may be pulsus paradoxus.
- Heart sounds are muffled or absent.
- Enlarged, tender liver.

Q: Name one **investigation** to confirm the diagnosis.

A: Echocardiography.

Q: Mention one **serious complication** of this. How would you manage it?

A: Cardiac tamponade. Managed by immediate paracentesis.

PERICARDIAL CALCIFICATION



Fig. A: Pericardial calcification.

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing:

- Calcified shadow at the left and lower border of the heart.
- Heart is enlarged in the transverse diameter.

Q: What is your radiological **diagnosis**?

A: Pericardial calcification.

Q: What is the **clinical diagnosis**?

A: Chronic constrictive pericarditis.

Q: Mention three **causes**.

A: As follows:

- TB.
- Hypercalcaemia as a result of any cause.
- Haemopericardium.

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest left lateral view showing flecks of calcification in the pericardium at the inferior and anterior borders.

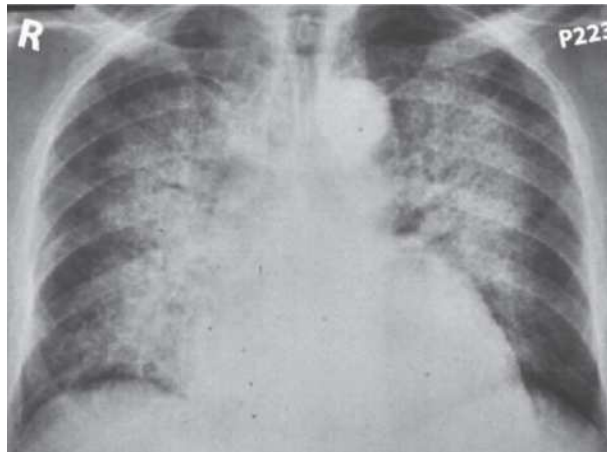
Q: What is your radiological **diagnosis**?

A: Pericardial calcification.



Fig. B: Pericardial calcification (lateral view).

PULMONARY OEDEMA



Pulmonary oedema.

Q: Write down the radiological **finding** of this X-ray.

A: CXR PA view showing:

- Fluffy or woolly opacities, spreading from both hilar regions, giving a butterfly or bat's wing appearance.
- Heart is enlarged in the transverse diameter.

Q: What is your radiological **diagnosis**?

A: Pulmonary oedema.

Q: Mention three **causes**.

A: As follows:

- Acute LVF as a result of any cause.
- Mitral stenosis.
- Excessive or rapid transfusion of fluid or blood.

Q: How to **manage**?

A: As follows:

- Propped-up position.
- Oxygen inhalation 4–6 L/min (60%–100%).
- Injection frusemide i.v.
- Injection morphine 10–20 mg i.v., with cyclizine or metoclopramide if vomiting.
- Angiotensin-converting-enzyme (ACE) inhibitor (captopril, lisinopril), vasodilator (isosorbide) and digoxin (in some cases).
- Treatment of primary cause.

PACEMAKER

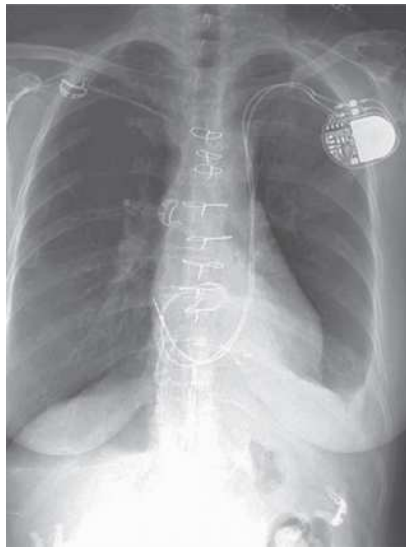


Fig. A: Dual-chamber pacemaker.

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing:

- Metallic suture wire of sternotomy.
- Dual-chamber pacemaker on the left side.

Q: What is your radiological **diagnosis**?

A: Dual-chamber pacemaker.

Q: Mention two common **indications**.

A: As follows:

- Complete heart block (with syncope or Stokes–Adams attack).
- Sick sinus syndrome.

Q: Mention five **complications**.

A: As follows:

- Infection.
- Displacement.
- Malfunction or pacemaker failure.
- Pacemaker-mediated tachycardia (by dual-chamber pacing).
- Pacemaker syndrome (occurs in single-chamber pacing).

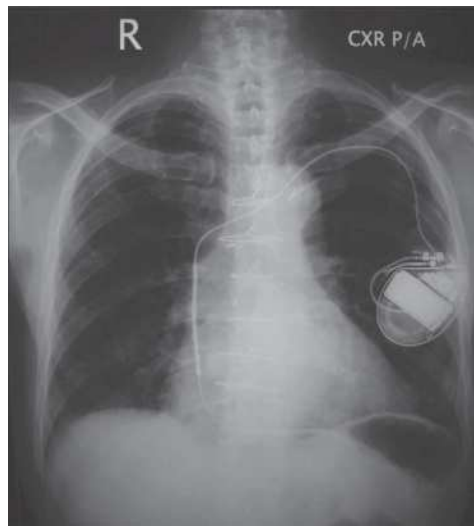


Fig. B: Single-chamber pacemaker.

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest PA view showing:

- Metallic suture wire of sternotomy.
- Single-chamber pacemaker on the left side.

Q: What is your radiological **diagnosis**?

A: Single-chamber pacemaker.

METALLIC PROSTHETIC VALVE



Fig. A: Metallic prosthetic mitral valve.

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray chest PA view showing:

- Metallic wire of the suture in the sternum (indicates sternotomy).
- A metallic prosthetic heart valve.

Q: What is your **radiological diagnosis**?

A: Metallic prosthetic mitral valve.

Q: Mention two **complications**.

A: As follows:

- Infective endocarditis.
- Valve failure.

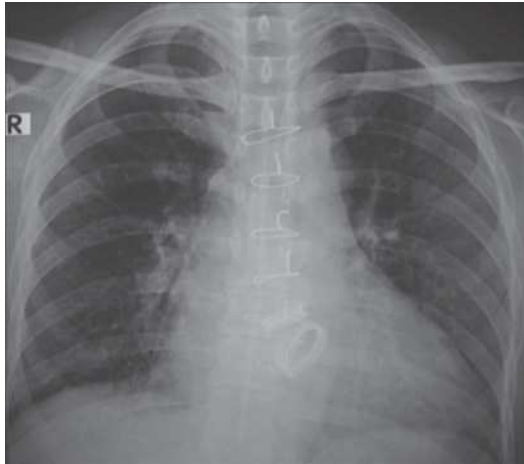


Fig. B: Metallic prosthetic mitral and aortic valves.

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray chest PA view showing:

- Metallic wire of the suture in the sternum (indicates sternotomy).
- Two metallic prosthetic heart valves.

Q: What is your **radiological** diagnosis?

A: Metallic prosthetic mitral and aortic valves.

ANKYLOSING SPONDYLITIS



Fig. A: Ankylosing spondylitis.

Q: What are your **findings** in the X-ray shown in Figure A?

A: X-ray of lumbosacral spine anteroposterior (AP) view showing:

- Calcification of anterior longitudinal and interspinous ligaments.
- There is syndesmophyte formation with bridging, giving rise to a bamboo-spine appearance.

Q: What is your radiological **diagnosis**?

A: Ankylosing spondylitis.

Q: Mention one **bedside test**.

A: Schober test.

Q: Write one **investigation** that is helpful for your diagnosis.

A: HLA-B27.



Fig. B: Ankylosing spondylitis.

Q: What are your **findings** in the X-ray shown in Figure B?

A: X-ray of lumbosacral spine lateral view showing:

- Syndesmophyte formation along the corners of the vertebral body with bridging, giving rise to a bamboo-spine appearance.
- Osteopaenia with marginal sclerosis of the vertebral body.

Q: What is your radiological **diagnosis**?

A: Ankylosing spondylitis.

POTT DISEASE



Pott disease.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray of dorsolumbar spine AP view showing:

- Reduction of the joint space between T6, T7 and also T8, with partial destruction of the vertebral body.
- Paravertebral shadow on both sides.
- There is marginal sclerosis.

Q: What is your radiological **diagnosis**?

A: Pott disease (TB of the spine or tuberculous spondylitis).

Q: Mention three **investigations**.

A: As follows:

- CBC count, ESR.
- X-ray chest PA view (to see the primary focus).
- Tuberculin test.
- Magnetic resonance imaging (MRI) of the thoracic spine.

Q: How to **confirm**?

A: CT or ultrasonography-guided FNAC.

MULTIPLE MYELOMA



Multiple myeloma.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray of the skull in lateral view showing multiple punched-out lytic lesions of variable sizes and shapes all over the skull.

Q: What is the most likely **diagnosis**?

A: Multiple myeloma.

Q: Write two important **differential** diagnoses.

A: As follows:

- Secondary deposit.
- Hyperparathyroidism.

Q: Name other investigations to **confirm** the diagnosis.

A: As follows:

- CBC count with ESR with peripheral blood film (PBF) (shows high ESR with a marked rouleaux formation).
- Bone marrow examination (shows atypical plasma cells).
- Plasma protein electrophoresis (shows M-band).
- Serum immunoelectrophoresis.
- Urine for Bence–Jones protein.

HEREDITARY HAEMOLYTIC ANAEMIA

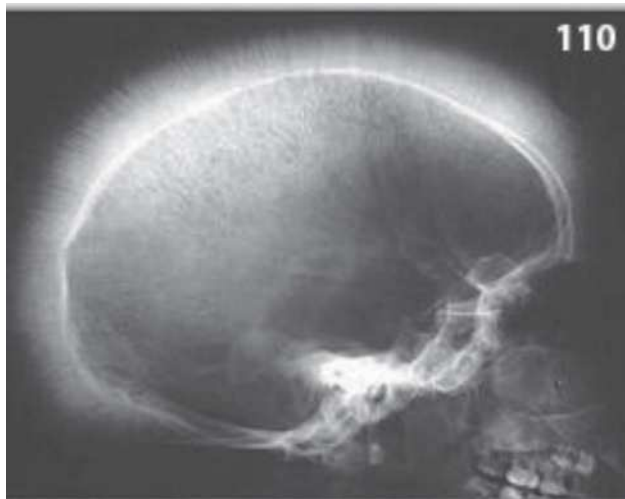


Fig. A: Thalassaemia.

Q: Write down the radiological **finding** of the X-ray shown in Figure A.

A: X-ray of the skull in lateral view showing:

- Widening of diploic space.
- Thinning of the outer table.
- Thickening and coarsening of trabeculae, giving rise to hair-on-end appearance.

Q: What is the most likely **diagnosis**?

A: Hereditary haemolytic anaemia, most likely α -thalassaemia major.

Q: Name four **examples**.

A: As follows:

- β -Thalassaemia major.
- Haemoglobin E disease (more common).
- Thalassaemia E disease (double heterozygous).
- Hereditary spherocytosis.

Q: Write down five important **physical findings** in this patient.

A: As follows:

- Anaemia.
- Jaundice.
- Splenomegaly.
- Frontal and parietal bossing.
- Mongoloid facies.

Q: Mention one **investigation** to confirm the diagnosis.

A: Haemoglobin electrophoresis.

Q: Mention one **simple investigation** helpful for the diagnosis.

A: CBC count with PBF (microcytic hypochromic anaemia).

Q: What **investigations** should be done in this patient?

A: As follows:

- CBC count with PBF (microcytic hypochromic anaemia).
- Reticulocyte count by supravital stain (usually high in haemolytic anaemia).
- Serum bilirubin (increased).
- Haemoglobin electrophoresis (shows absent or grossly reduced HbA and increased HbF in α -thalassaemia major. In case of β -thalassaemia minor, HbA2 is increased).



Fig. B: X-ray of hands in hereditary haemolytic anaemia.

Q: Write down the radiological **finding** of the X-ray shown in Figure B.

A: X-ray of both hands in AP view showing:

- Widening of the medullary cavity.
- Thinning of the cortex.
- Reduction in the number of trabeculae and thickening of remaining trabeculae.
- Generalized osteopaenia.

Q: What is the most likely **diagnosis**?

A: Hereditary haemolytic anaemia.

ACROMEGALY



Acromegaly.

Q: What are your radiological findings?

A: X-ray of the skull in lateral view showing:

- Skull is enlarged.
- Frontal sinus is enlarged.
- Sella turcica is enlarged.
- There is erosion of the anterior and posterior clinoid processes.

Q: What is your radiological diagnosis?

A: Acromegaly (as a result of pituitary adenoma).

Q: What other investigations should be done.

A: As follows:

- X-ray of hands and feet (to see the heel pad).
- MRI of the skull.
- Growth hormone (GH) assay (radioimmunoassay).
- Glucose tolerance test with simultaneous measurement of GH.
- Measurement of insulin-like growth factor-1 (IGF-1) (also called somatomedin C).
- Assessment of other anterior pituitary hormones.
- Perimetry (bitemporal hemianopia).

Q: Mention one specific treatment.

A: Trans-sphenoidal removal of adenoma.

Q: Mention two drugs that can be used.

A: As follows:

- Somatostatin analogue, e.g., octreotide or lanreotide.
- Bromocriptine (dopamine agonist).
- Pegvisomant (a peptide GH receptor antagonist).

TOPHI



Tophi.

Q: What are your radiological findings?

A: X-ray of the left foot showing:

- Two bony outgrowths—one large involving the first metatarsophalangeal (MTP) joint and one small in the second distal interphalangeal (DIP) joint.
- Presence of lytic lesion.
- Destruction of the first interphalangeal joint.

Q: What is your radiological diagnosis?

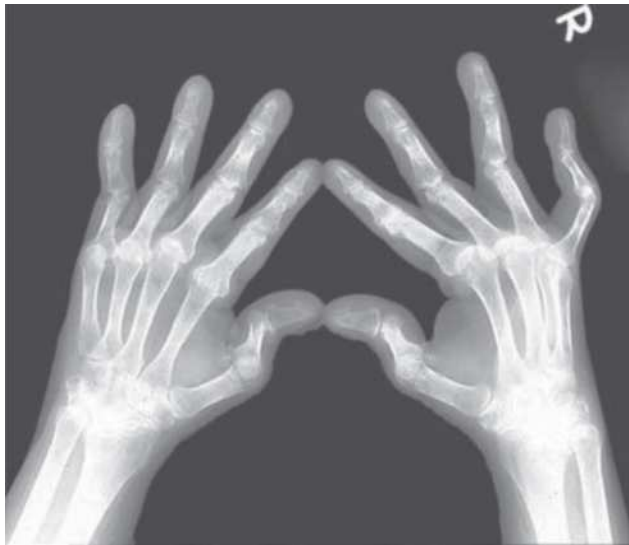
A: Chronic tophaceous gout.

Q: How to confirm your diagnosis?

A: As follows:

- Aspiration of fluid or tophi to see monosodium urate monohydrate (MSUM) crystals under the polarized microscope (needle-shaped, negatively birefringent crystals).
- Serum uric acid (high).

RHEUMATOID HAND



Rheumatoid hand.

Q: Write down the radiological findings of this X-ray.

A: X-ray of both hands in AP view showing:

- Reduction of all joint spaces.
- Periarticular osteopaenia involving metacarpophalangeal and wrist joints of both hands.
- Disorganisation of all proximal interphalangeal (PIP) joints of both hands.
- 'Z'-deformity of the thumb.
- Ulnar deviation of both hands.

Q: What is your radiological diagnosis?

A: Rheumatoid arthritis.

Q: Mention five bad prognostic factors of this disease.

A: As follows:

- Higher baseline disability.
- Female gender.
- Involvement of MTP joints.
- Positive rheumatoid factor.
- Disease duration of over 3 months.

Q: Mention five investigations.

A: As follows:

- CBC count with ESR (high ESR, anaemia).
- RA and Rose–Waler (RW) tests.
- Anticyclic citrullinated peptide (anti-CCP) antibody (helpful for early diagnosis, highly specific for RA).
- X-ray chest (to see diffuse parenchymal lung disease [DPLD], Caplan syndrome).
- C-reactive protein (CRP) (high).

Q: What are the principles of treatment?

A: As follows:

- Relief of symptoms: Rest, nonsteroidal anti-inflammatory drug (NSAID), physiotherapy, explanation and reassurance.
- Suppression of activity and progression of disease by disease-modifying antirheumatic drugs (DMARDs) (methotrexate, sulphasalazine, hydroxychloroquine, leflunomide etc.).
- Biological agents (rituximab, tocilizumab etc.).
- Restoration of function of affected joints.

RESORPTION OF TERMINAL PHALANGES



Resorption of terminal phalanges.

Q: What are your radiological **findings**?

A: X-ray of both hands in AP view showing:

- Periarticular osteopaenia.
- Tapering of terminal phalanges.
- Resorption of distal phalanges of fingers.
- There is calcification at the tip of the left index and the right thumb.

Q: What is your probable **diagnosis**?

A: Systemic sclerosis.

Q: What is the likely **cause** in this case?

A: CRST or CREST syndrome.

RICKETS



Fig. A: Rickets.

Q: Write down the radiological **findings** of the X-ray shown in Figure A.

A: X-ray of both hands in AP view showing:

- Widening, splaying, cupping and irregularity of metaphysis.
- Distance between epiphysis and metaphysis is increased (zone of provisional calcification is lost).

Q: What is your radiological **diagnosis**?

A: Rickets.

Q: Mention three other **investigations**.

A: As follows:

- X-ray of elbows and knees.
- Serum calcium and phosphate (both are low).
- Serum alkaline phosphatase (high).
- Serum 25-hydroxyproline (low or absent).

Q: How to **treat**?

A: As follows:

- 25-Hydroxycholecalciferol 50 mcg daily, or active vitamin D metabolite (1- α -hydroxycholecalciferol) 1–2 mcg daily, or 1,25 dihydroxycholecalciferol 0.25–1.5 mcg daily.
- **Plus** calcium 500–1000 mg daily. A higher dose may be required in patients with malabsorption.
- Adequate exposure to sunlight.
- Dietary supplement.



Fig. B: Rickets.

Q: Write down the radiological **findings** of the X-ray shown in Figure B.

A: X-ray of the leg including the knee joint and ankle joint showing:

- Widening, splaying, cupping and irregularity of metaphysis.
- Distance between epiphysis and metaphysis is increased (zone of provisional calcification is lost).
- Bowing of tibia and fibula.

Q: What is your radiological **diagnosis**?

A: Rickets.

SCURVY



Scurvy.

Q: Write down the radiological **findings** of this X-ray.

A: X-ray of the knee including the lower end of femur and the upper end of tibia–fibula showing:

- Epiphysis as ring-shaped, sclerotic and sharply margined called Wimberger sign.
- Metaphysis is dense (zone of provisional calcification), giving a white line called Frankel line.
- Beneath this line, there is a lucent zone called Trummerfeld zone.
- At the corner, there is a spur called Pelkan spur.

Q: What is your radiological **diagnosis**?

A: Scurvy.

Q: What are the **causes**?

A: As follows:

- Dietary deficiency—lack of fruits and fresh vegetables in children older than 2 months.
- In infants—delayed weaning, lack of fruit juice, deficiency in the lactating mother.

Q: How to **treat**?

A: As follows:

- Vitamin C 250 mg—three to four times daily orally.
- Dietary supplements, especially fresh fruits (orange, mango, pineapple, guava etc.) and liver extract.
- Bottle-fed infants should be given fruit juice. Nursing mothers should take sufficient vitamin C, which is secreted in the breast milk.

AVASCULAR NECROSIS OF FEMORAL HEAD



Avascular necrosis of the femoral head.

Q: Write down the radiological **finding** of this X-ray.

A: X-ray of the pelvis in AP view showing:

- Rarefaction and sclerotic small head of the left femur.
- Joint space between the head and the acetabulum is increased.

Q: What is your radiological **diagnosis**?

A: Avascular necrosis of the head of the left femur (called osteonecrosis).

Q: What is the **presentation**?

A: Pain in the hip and difficulty in walking.

Q: How to **confirm** your diagnoses?

A: As follows:

- X-ray (may be normal in the early stage).
- MRI—more confirmatory (100%).
- Bone scan—increased uptake (helpful in the early stage).

Q: Mention five **causes**.

A: As follows:

- Prolonged steroid therapy (other drug—prolonged use of heparin).
- Cushing syndrome.
- Osteoporosis.
- Alcohol abuse.
- Collagen disease (SLE, RA, systemic sclerosis, vasculitis).

N.B. Other causes are:

- *Sickle cell anaemia (and other haemoglobinopathies).*
- *Exposure to high barometric pressure—in deep sea divers (Caisson disease) and tunnel workers.*
- *Perthes disease.*
- *Radiation therapy.*
- *Post-traumatic.*

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)



ERCP showing *Ascaris lumbricoides* in the common bile duct.

Q: What are your **findings**?

A: This is an ERCP showing a linear translucent shadow within the common bile duct.

Q: What is your **diagnosis**?

A: Round worm in the common bile duct.

Q: How does the patient **present**?

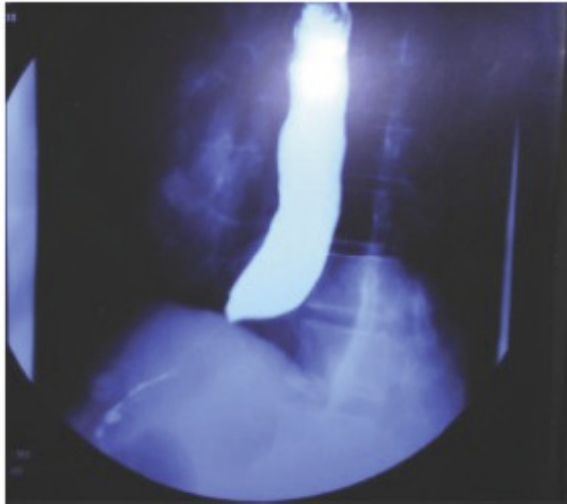
A: As follows:

- Upper abdominal pain, mostly in the right hypochondrium.
- Features of obstructive jaundice and cholangitis.

Q: How to **treat** such a case?

A: The worm is removed during ERCP.

ACHALASIA CARDIA



Achalasia cardia.

Q: Write down the radiological **finding** of this X-ray.

A: Barium swallow of the oesophagus showing:

- Dilatation of the oesophagus with smooth tapering of its lower end.
- Absence of fundal gas.

Q: What is your radiological **diagnosis**?

A: Achalasia cardia.

Q: Mention one **investigation** to confirm your diagnosis.

A: Oesophageal manometry.

Q: Mention three **complications**.

A: As follows:

- Oesophageal carcinoma.
- Aspiration pneumonia
- Malnutrition.

Q: How to **treat**?

A: As follows:

- Endoscopic dilatation by a pneumatic bougie.
- Heller cardiomyotomy.

CARCINOMA OF OESOPHAGUS

Carcinoma of oesophagus.

Q: Write down the radiological **finding** of this X-ray.

A: Barium swallow of the oesophagus showing an irregular filling defect at the lower end of the oesophagus.

Q: What is your radiological **diagnosis**?

A: Carcinoma of the oesophagus.

Q: Mention one investigation to **confirm** your diagnosis.

A: Endoscopy and biopsy.

CARCINOMA OF STOMACH



Carcinoma of stomach.

Q: Write down the radiological **finding** of this X-ray.

A: Barium meal X-ray of the stomach showing an irregular filling defect at the distal part of the stomach.

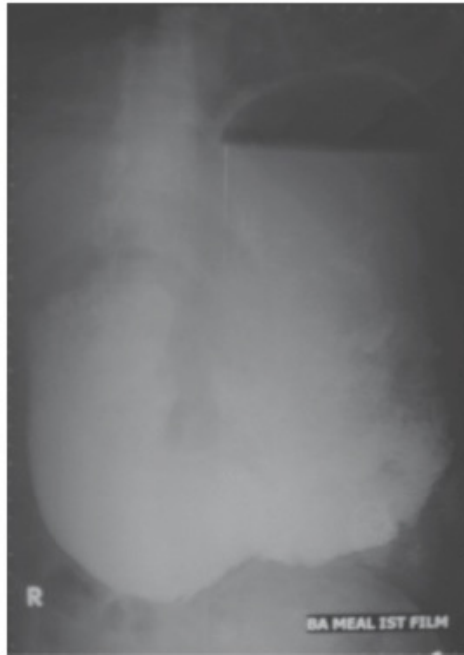
Q: What is your radiological **diagnosis**?

A: Carcinoma of stomach.

Q: Mention one investigation to **confirm** your diagnosis.

A: Endoscopy and biopsy.

GASTRIC OUTLET OBSTRUCTION



Gastric outlet obstruction.

Q: Write down the radiological **finding** of this X-ray.

A: Barium meal X-ray of the stomach showing:

- Stomach is hugely dilated with food residue.
- Dye is not passing beyond the pylorus.

Q: What is your radiological **diagnosis**?

A: Gastric outlet obstruction.

Q: What is the likely **cause**?

A: Chronic duodenal ulcer with pyloric stenosis.

Q: What other **investigations** do you suggest?

A: Endoscopy and biopsy.

Q: What is the **treatment option**?

A: Gastrojejunostomy with vagotomy.

Q: Name one physical **sign**.

A: Visible peristalsis from left to right in the upper abdomen.

Q: Mention one **symptom**.

A: Projectile or induced vomiting.

PANCREATIC CALCIFICATION



Pancreatic calcification.

Q: Write down the radiological **finding** of this X-ray.

A: Plain X-ray of the abdomen showing multiple calcified shadows superimposed on the vertebral column and also on the left side along the anatomical distribution of the pancreas.

Q: What is your radiological **diagnosis**?

A: Pancreatic calcification.

Q: What is the underlying **diagnosis**?

A: Chronic pancreatitis.

Q: Mention three **causes**.

A: As follows:

- Chronic pancreatitis, commonly alcoholic.
- Fibrocalcific pancreatic disease (FCPD).
- Hereditary pancreatitis.
- Hypercalcaemia as a result of any cause.
- Haemochromatosis.
- Idiopathic chronic pancreatitis.
- Posttraumatic pancreatitis.

Q: Mention five further **investigations**.

A: As follows:

- Ultrasonography.
- CT scan or MRI of the abdomen.
- Magnetic resonance cholangiopancreatography (MRCP).
- ERCP.
- Pancreatic function test.

POLYCYSTIC KIDNEY DISEASE



Polycystic kidney disease.

Q: Write down the radiological **finding** of this X-ray.

A: Intravenous urogram (IVU) showing:

- Enlargement of both kidneys—left one larger than the right.
- Distortion, stretching and elongation of the pelvicalyceal system, giving rise to a spidery appearance.
- Left ureter is dilated and shifted medially towards the vertebral column.

Q: What is your radiological **diagnosis**?

A: Polycystic kidney disease.

Q: Mention a single **investigation**.

A: Ultrasonography of both kidneys.

Q: If the patient is **unconscious**, what is the likely **diagnosis**?

A: Subarachnoid haemorrhage (as a result of rupture of berry aneurysm).

Q: Mention **one treatment**.

A: Ultrasonic-guided aspiration of a large cyst.

CT SCAN

CT scan is a radiological procedure that uses X-ray and a computer to produce a series of cross-sectional images of the inside of the body.

Uses:

- To diagnose internal injuries, bleeding, mass lesion etc.
- To diagnose various rheumatological conditions including bone loss, joint deformity, calcification etc.
- To guide procedures such as surgery, biopsy and radiation therapy.
- To monitor progression of various diseases such as lung nodule, cancer etc.
- Contrast CT scan is used to assess the vascularity and nature of a lesion.
- CT angiogram is used to evaluate the vascular system of an organ.

Advantages:

- Higher image resolution than X-ray.
- Noninvasive technique.
- May be used in situations where MRI is contraindicated.
- Cheaper than MRI and many other imaging modalities.
- Quicker than MRI and many other imaging modalities, so it is very useful for quick screening in emergency conditions such as subarachnoid haemorrhage.

Advantages of multislice CT over helical CT:

- Increased speed and ability to perform volume acquisition.
- Multislice CT allows faster scanning, thinner sections or larger scan ranges, which lead to less motion artefact, especially in critically ill patients, children and trauma patients.
- Helical CT is a continuous volume acquisition that ensures that no lesions are lost because of respiration or after motion-related artefact. The prime advantage of volume acquisition is the improved three-dimensional capability.

Disadvantages of CT scan:

- Exposure to radiation.
- Reaction to contrast materials if contrast CT scan is performed.
- Image quality is lower than that by MRI.
- Poor visualization of infarction.

MRI SCAN

MRI is a nonionizing imaging technique using magnetic fields and radiofrequency waves to visualize the internal anatomical structures.

Uses:

- To diagnose internal injuries, infarction, mass lesion etc.
- To diagnose defect with myelination (e.g., multiple sclerosis).
- To diagnose diseases of the spine and the spinal cord.
- Contrast MRI is used to assess the vascularity and nature of a lesion.
- Magnetic resonance angiography (MRA) is used to evaluate the vascular system of an organ.
- Functional MRI (fMRI) of the brain can be used to identify important language and movement control areas in the brain in people who are being considered for brain surgery.

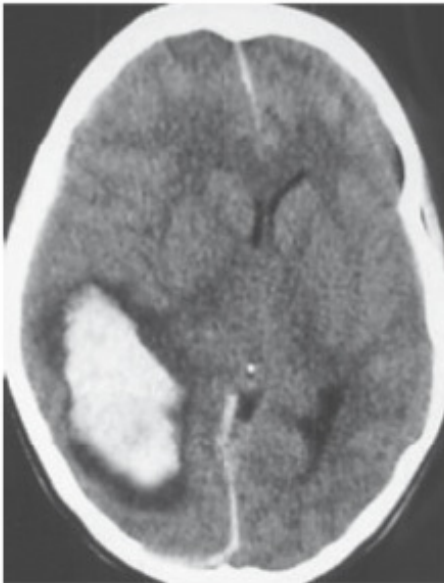
Advantages:

- High-resolution imaging.
- Images of the brain, other cranial structures and the spine are more clear and detailed than that with other imaging methods. So, MRI is very useful in early diagnosis and evaluation of intracranial and spinal disorders including tumours.
- It enables the detection of abnormalities that might be obscured by a bone with other imaging methods.
- Direct multiplanar imaging in transverse, coronal and sagittal planes or in any other desired plane is possible.
- Free from ionizing radiation. So, safe for pregnant women and children.
- Contrast material used in MRI is less likely to produce an allergic reaction than that by the iodine-based materials used for conventional X-ray and CT scanning.
- Noninvasive technique.

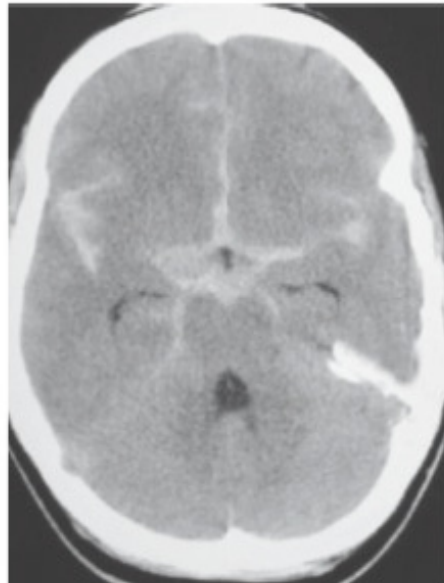
Disadvantages:

- Patients with electronic devices (e.g., cardiac pacemaker, implantable heart defibrillator etc.), metallic implant (e.g., metallic valve, joint prostheses etc.) or metallic artificial life support cannot be scanned by MRI because of strong magnetic fields.
- Scanning is time consuming.
- Movement degrades image.
- More expensive.
- Allergic reaction to contrast material may occur rarely (especially in patients with kidney problem who are on dialysis).
- Difficult to perform in claustrophobic patients.

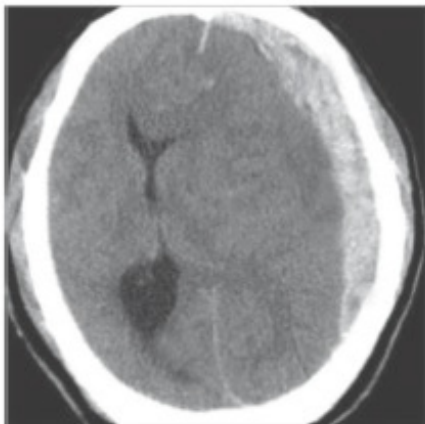
FEW COMMON CT SCANS



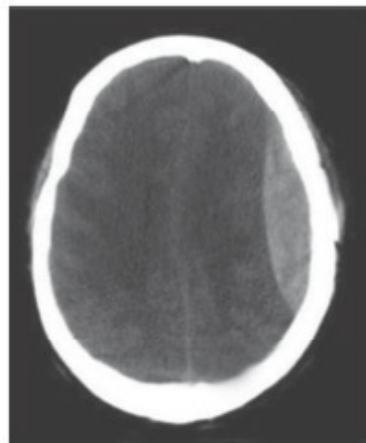
CT scan of the brain shows a hyperdense lesion in the right parietal lobe with perilesional oedema. The diagnosis is **intracerebral haemorrhage** in the right parietal lobe.



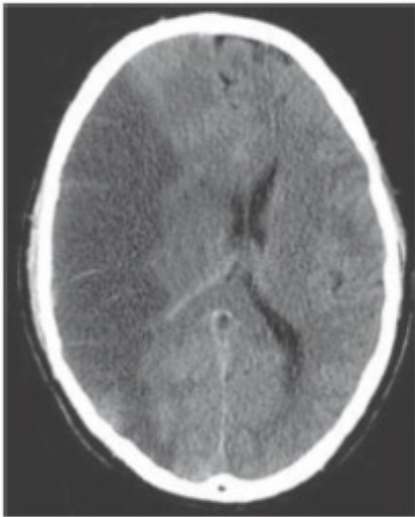
CT scan of the head shows high attenuation (white areas) with obliteration of the ventricles. The diagnosis is **subarachnoid haemorrhage**.



CT scan of the head shows crescent-shaped hyperdense extracerebral collection within the subdural space. The diagnosis is **subdural haematoma** on the left side.



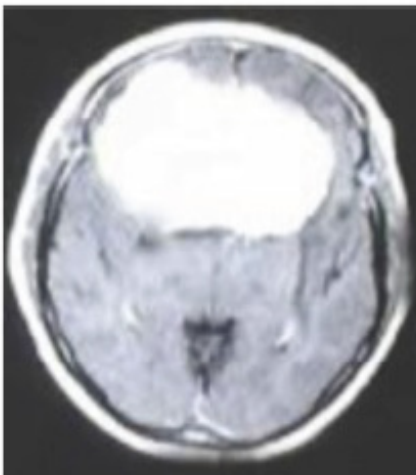
CT scan of the head shows a high-density biconvex area. The diagnosis is **extradural haematoma** on the left side.



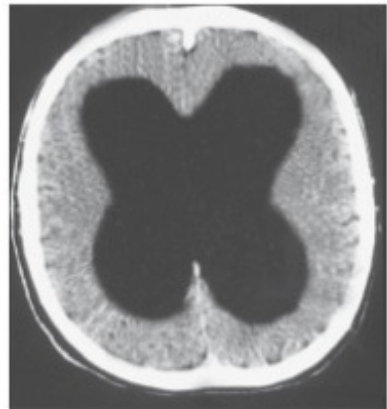
CT scan of the brain shows a hypodense area on the right side with shifting of the ventricle to the left side. The diagnosis is **right-sided cerebral infarction**.



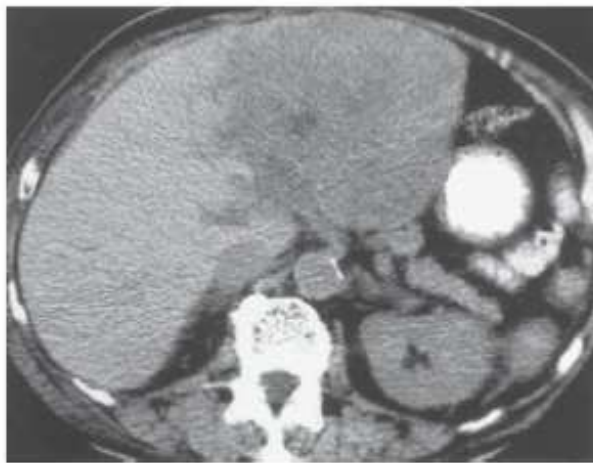
Contrast CT scan of the head showing a ring-like cystic hypodense lesion on the right parietal lobe. The diagnosis is **cerebral abscess**.



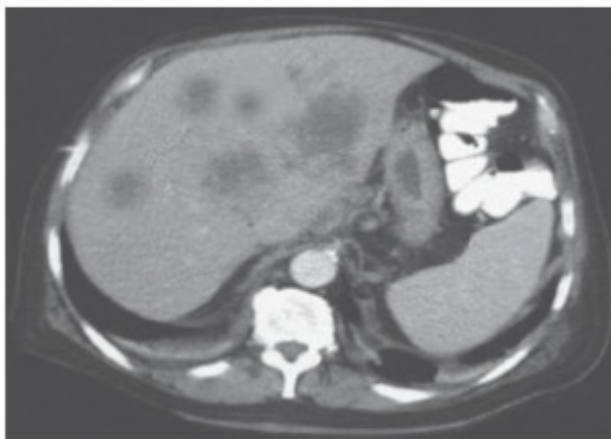
CT scan of the head shows a hyperdense, irregular mass in the frontal region. The diagnosis is **meningioma**.



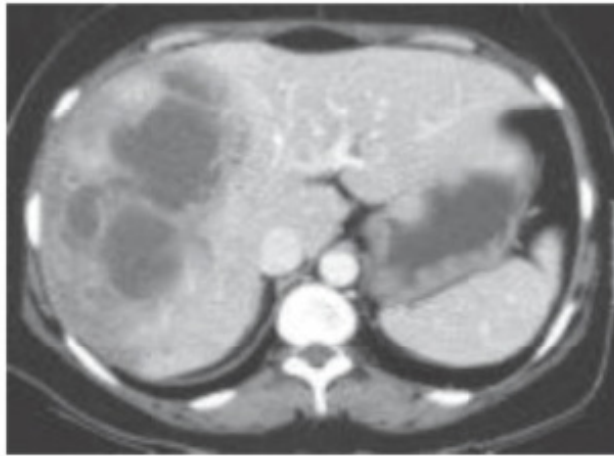
CT scan of the head shows marked dilatation of both lateral ventricles with thinned brain tissue outside the hypodense area. The diagnosis is **hydrocephalus**.



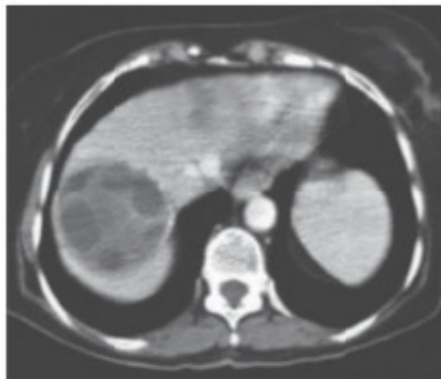
CT scan of the abdomen shows an irregular hypodense mass in the left lobe of the liver.
The diagnosis is **hepatoma**.



CT scan of the abdomen shows multiple hypodense areas within both right and left lobes of the liver. The diagnosis is **multiple secondaries in the liver**.



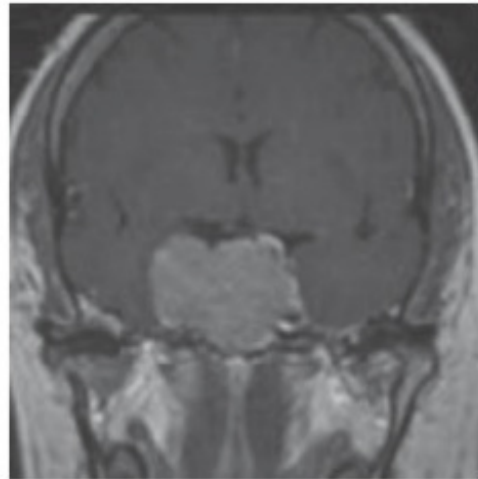
CT scan of the abdomen shows multiple hypodense areas with ragged irregular margin within the right lobe of the liver. The diagnosis is multiple **liver abscesses**.



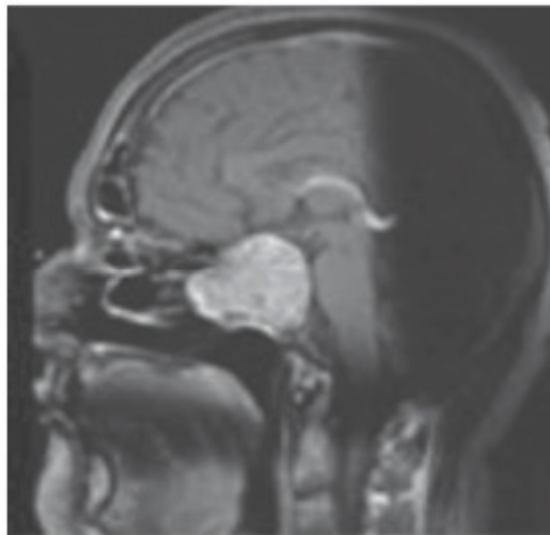
CT scan of the abdomen shows a large, hypodense cystic lesion with septation within the right lobe of the liver. The diagnosis is **hydatid cyst in the liver**.



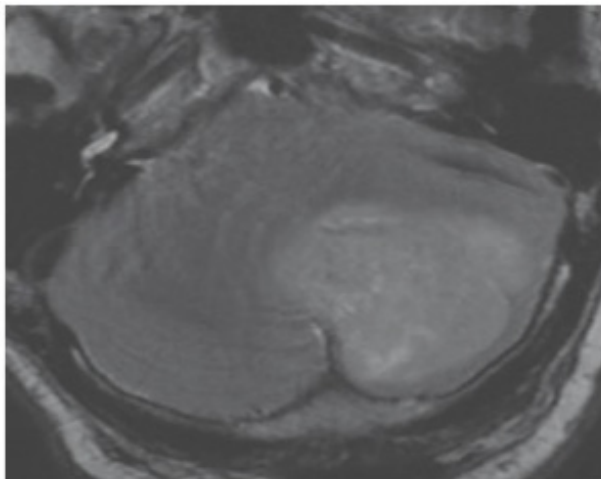
MRI of the dorsolumbar spine lateral view showing destruction of the L2 and L3 vertebral bodies with reduction of the joint space. The diagnosis is **Pott disease**.



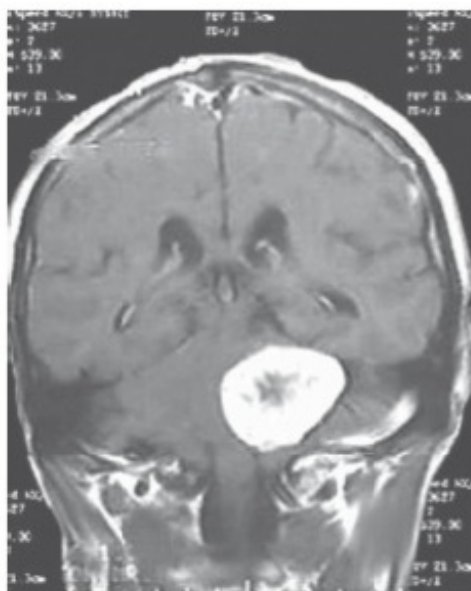
MRI of brain sagittal view shows a large, irregular, hyperdense area in pituitary fossa. The diagnosis is **pituitary macroadenoma**.



MRI of brain coronal view shows a large, irregular, hyperdense area in pituitary fossa. The diagnosis is **pituitary macroadenoma**.



MRI of brain shows a large, hyperintense mass in the left cerebellar hemisphere.
The diagnosis is **cerebellar tumour**.



MRI of the brain showing a mixed hyperintense mass in the left cerebellopontine angle.
The diagnosis is **acoustic neuroma**.

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ECG

15

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'A good start is a good help'
—The Author

BASIC CONCEPT OF ECG

Electrocardiogram (ECG) is the graphical representation of electrical potentials that are produced when the electric current passes through the heart.

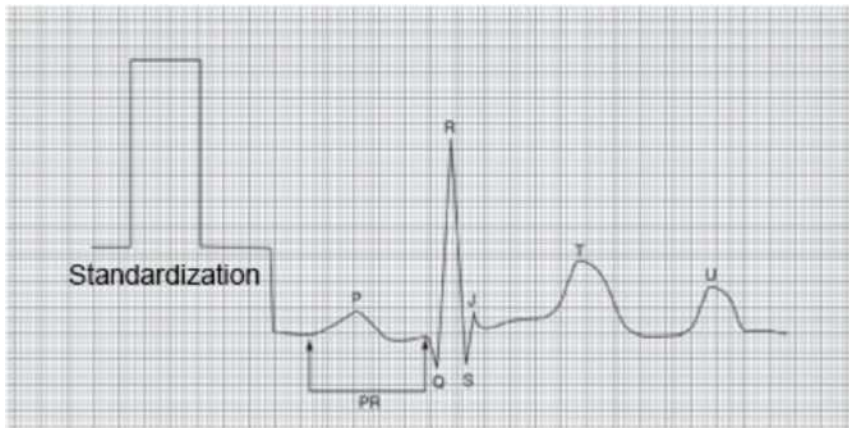
WAVES IN ECG

ECG records the electrical impulse as waves or deflections on the ECG paper. One beat is recorded as a group of waves (P–QRS–T).

1. P: Represents atrial depolarization.
2. P–R interval: Represents the time taken for the cardiac impulse to spread from SA node to the ventricles.
3. QRS complex: Represents ventricular depolarization.
 - Q(q): First negative deflection before R-wave.
 - R(r): First positive deflection.
 - S(s): Negative deflection after R-wave.
4. T-wave: Represents ventricular repolarization.

Other waves:

1. J: At the beginning of ST segment.
2. U: Found after T-wave, preceding the next P-wave.



Waves in ECG tracing

LEADS

In a normal ECG recording, there are 12 leads—three bipolar standard leads, three unipolar limb leads and six chest leads.

1. Bipolar standard leads (limb leads) designated as LI, LII and LIII.

- LI: Difference of potential between the left arm and the right arm (LA and RA).
- LII: Difference of potential between the right arm and the left leg (RA and LL).
- LIII: Difference of potential between the left arm and the left leg (LA and LL).

2. Unipolar limb leads (augmented limb leads) designated as augmented vector right (AVr), augmented vector left (AVI) and augmented vector foot (AVf). These leads have a very low voltage that cannot be recorded clearly. So, recordings from these leads are increased in amplitude called augmented unipolar leads.

- AVr: Augmented unipolar right arm (RA) lead. Records the changes of potential occurring in the part of the heart facing towards the right shoulder.
- AVI: Augmented unipolar left arm (LA) lead. Records the changes of potential of the heart facing towards the left shoulder.
- AVf: Augmented unipolar left leg (LL) lead. Records the changes of potential of the heart facing towards the left hip.

3. Chest Leads (unipolar) Designated by 'V'. Electrodes are placed in the following places on the chest wall:

- V1: Fourth intercostal space at the right sternal border.
- V2: Fourth intercostal space at the left sternal border.
- V3: Midway between V2 and V4 lead on the left side.
- V4: Fifth intercostal space in the left midclavicular line.
- V5: Fifth intercostal space in the left anterior axillary line.
- V6: Fifth intercostal space in the left midaxillary line.

View of the heart in all leads:

- LI, AVI, V5 and V6: Reflects the lateral (or anterolateral) aspect of the heart.
- LII, LIII and AVf: Reflects inferior aspect of the heart.
- V1 and V2: Reflects the right ventricle.
- V3 and V4: Reflects the interventricular septum.
- V5 and V6: Reflects the left ventricle.
- V1–V6: Reflects the anterior aspect of the heart.
- LI, AVI, V1–V6: Reflects the extensive anterior or anterolateral aspect of the heart.
- LI and AVI: High lateral.
- LII, LIII, AVf, LI, AVI, V5 and V6: Inferolateral.

INTERPRETATION OF ECG

Before interpretation, one must know details about the ECG paper, standardization and different waves in ECG.

Look at the following points carefully:

1. Standardization (see in the beginning): This is 10 mm (1 mV).
2. Paper speed: 25 mm/s.
3. Rhythm: See R–R interval (R-wave to R-wave interval), regular or irregular (LII is called rhythm lead).
4. Count the heart rate.
5. Different waves:
 - P: Normal, small or tall, inverted, wide, notched, bifid, variable configuration.
 - P–R interval: Normal or prolonged or short.
 - Q: Normal or pathological.
 - R: Normal or tall or short, notched or M-pattern.
 - QRS complex: Normal or wide, high or low voltage, variable or change of shape.
 - ST segment: Elevated or depressed.
 - T: Normal or tall or small or inverted.
 - U-wave: Normal or small.
 - QT: Short or prolonged.
6. Axis: Whether normal or right- or left-axis deviation.
7. Abnormalities: Any arrhythmia, infarction, hypertrophy.

Q: What are the diseases diagnosed by looking at an ECG?

A: As follows:

- Tachycardia or bradycardia.
- Chamber enlargement.
- Myocardial infarction.
- Arrhythmias.
- Block (first-degree block, sinoatrial block [SA block], atrioventricular block [AV block], bundle branch block).
- Drug effect (such as digoxin).
- Extracardiac abnormalities: Electrolyte imbalance (such as hypo- or hyperkalaemia), hypo- or hypercalcaemia, low-voltage tracing (in myxoedema, hypothermia, emphysema).
- Exercise ECG to see coronary artery disease.

ECG PAPER

ECG paper shows small and large squares. In each small square, thin horizontal and vertical lines are present at 1-mm interval. A heavier, thick line is present at every 5-mm (five small squares) interval. Time is measured horizontally, and height is measured vertically.

1. One small square:
 - Height = 1 mm.
 - Horizontal (in time) = 0.04 seconds.

2. One big square (five small squares):

- Height = 5 mm.
- Horizontal (in time) = $0.04 \times 5 \text{ seconds} = 0.2 \text{ seconds}$.
So, 0.2 seconds = 5 mm.
1 second = $5/0.2 = 25 \text{ mm}$.
So, recording speed is 25 mm/s (i.e., 1500 mm/min).

3. Isoelectric line: It is the base line in the ECG paper. Waves are measured either above (positive deflection) or below (negative deflection).

STANDARDIZATION OF ECG

- Normally, 1-mV current: 10-mm height (10 small squares).
- Half strength: 5 mm.
- Recording speed: 25 mm/s (i.e., 1500 mm/min).

Before telling **low voltage or high voltage**, see the normal standardization (i.e., 10 mm in height).

Criteria of low-voltage tracing:

- In standard limb leads: QRS complex <5 mm (mainly R-wave).
- In chest leads: QRS complex <10 mm (mainly R-wave).

Remember the following points:

- Depolarization indicates initial spread of stimulus through the muscle, causing activation or contraction.
- Repolarization indicates return of the stimulated muscle to the resting state (recovery from activation or contraction).
- Depolarization towards the electrode: Positive deflection (above the isoelectric line).
- Depolarization away from the electrode: Negative deflection (below the isoelectric line).
- Rhythm: Interval between two successive R–R.

NORMAL ECG

Characteristics of normal ECG:

- Normal ECG consists of P-wave (atrial beat), followed by QRS complex, ST- and T-wave (ventricular beat).
- Capital letters P, Q, R, S, T: Indicate large wave (>5 mm).
- Small letters p, q, r, s, t: Indicate small wave (<5 mm).

Intervals and segment in ECG

- P–R interval: Distance between the beginning of P and beginning of QRS (Q).
- P–P interval: Distance between two successive P-waves. In sinus rhythm, P–P interval is regular.
- R–R interval: Distance between two successive R-waves.
- Q–T interval: Distance interval between the beginning of Q-wave and the end of T-wave.
- ST segment: Distance from the end of QRS complex to the beginning of T-wave. It indicates the beginning of ventricular repolarization. Normally, it is in the isoelectric line but may vary from -0.5 to $+2$ mm in chest leads.

DETAILS OF WAVES AND INTERVALS

P-WAVE

Characters of normal P-wave:

- P-wave is better seen in LII (also seen in V1).
- Normal P is rounded—neither peaked nor notched.
- Width or duration (in time, horizontally): 0.10 seconds (2.5 small squares).
- Height: 2.5 mm (2.5 small squares) height $\times$ duration = 2.5×2.5 small squares.
- P-wave is upright in all leads, mainly LI, LII and AVf (except AVr. P is inverted in AVr and occasionally in AVI).
- P-wave in V1 may be biphasic (equal upward and downward deflection), notched and wide (activation of the right atrium produces a positive component and activation of the left atrium produces a negative component).

Abnormalities of P-wave: It may be absent, tall or small, wide, notched, biphasic, inverted, variable, multiple.

Causes of absent P-wave:

- Atrial fibrillation (P is absent or replaced by fibrillary **f**-wave).
- Atrial flutter (P is replaced by flutter wave, which shows a **sawtooth** appearance).
- SA block or sinus arrest.
- Nodal rhythm (usually abnormal, small P-wave).
- Ventricular ectopic and ventricular tachycardia.
- Supraventricular tachycardia (SVT) (P-wave is hidden within QRS complex as a result of tachycardia).
- Hyperkalaemia.
- Idioventricular rhythm.

Causes of tall P-wave:

- Tall P-wave is called P pulmonale (height >2.5 mm, i.e., >2.5 small squares).
- It is because of right atrial hypertrophy or enlargement.

Causes of small P-wave:

- Atrial tachycardia.
- Atrial ectopic.
- Nodal rhythm (high nodal).
- Nodal ectopic (high nodal).

Causes of wide P-wave:

- Broad and notched P-wave is called P mitrale (duration >0.11 seconds or >2.5 small squares).
- It is because of left atrial hypertrophy or enlargement.
- In V1, P-wave may be biphasic, with a small positive wave preceding a deep and broad negative wave (indicates left atrial enlargement or hypertrophy).

Causes of inverted P-wave (negative in LI, LII and AVf):

- Incorrectly placed leads (reversed arm electrodes).
- Dextrocardia.
- Nodal rhythm with retrograde conduction.
- Low atrial and high nodal ectopic beats.

Causes of variable P-waves:

- Presence of variable P-waves indicates wandering pacemaker.

Causes of multiple P-waves (consecutive two or more):

- AV block (either partial or complete heart block).
- SVT with AV block.

P–R INTERVAL

Characters of normal P–R interval:

- Normal P–R interval: 0.12–0.20 seconds (maximum of five small squares).
 - In children, upper limit is 0.16 seconds.
 - In adolescent, upper limit is 0.18 seconds.
 - In adult, upper limit is 0.22 seconds.
- P–R interval is short, if it is <0.10 seconds and long, if it is >0.22 seconds.

Abnormalities of P–R Interval: It may be prolonged, short and variable.

Prolonged P–R interval (>0.2 seconds): It is because of first-degree heart block. Causes are:

- Ischaemic heart disease (occasionally, inferior myocardial infarction).
- Acute rheumatic carditis.
- Myocarditis (as a result of any cause).
- Atrial dilatation or hypertrophy.
- Hypokalaemia.
- Drugs: Digitalis toxicity, quinidine, occasionally β -blocker, calcium channel blocker (verapamil).

Short P–R interval (<0.12 seconds): Causes are:

- Wolff–Parkinson–White (WPW) syndrome: In this case, there is a δ -wave.
- Lown–Ganong–Levine (LGL) syndrome: In this case, there is no δ -wave.
- Nodal rhythm.
- Nodal ectopic (high nodal).
- Occasionally, if dissociated beat is present, and also in infant, steroid therapy is used.

Variable P–R interval: Causes are:

- Wenckebach phenomenon (Mobitz type I): There is progressive lengthening of P–R interval, followed by a drop beat.
- Partial heart block (Mobitz type II): P–R interval is fixed and normal, but sometimes P-wave is not followed by QRS complex.
- 2:1 AV block: Alternate P-wave is not followed by QRS complex.

- Complete AV block: No relation between P-wave and QRS complex.
- Wandering pacemaker: Variable configuration of P-wave.

Q-WAVE

Characters of normal Q-wave:

- Q-wave is usually absent in most of the leads. However, small Q-wave may be present in I, II, AVI, V5 and V6. This is because of septal depolarization.
- Small q may be present in LIII (which disappears with inspiration).
- Depth: <2 mm (two small squares).
- Width: One small square.
- It is 25% or less in amplitude of the following R-wave in the same lead.

Characters of pathological Q-wave:

- Deep >2 mm (two small squares).
- Wide >0.04 seconds or more (>1 mm or one small square).
- Should be present in more than one lead.
- Associated with loss of height of R-wave.
- Q-wave should be $>25\%$ of the following R-wave of the same lead.

Causes of pathological Q-wave:

- Myocardial infarction (commonest cause).
- Ventricular hypertrophy (left or right).
- Cardiomyopathy.
- Left bundle branch block (LBBB).
- Emphysema (as a result of axis change or cardiac rotation).
- Q-wave only in LIII is associated with pulmonary embolism (SI, QIII and TIII pattern).

N.B. Remember the following points:

- *Q-wave in V1, V2 and V3 may be seen in left ventricular hypertrophy (LVH), confused with old myocardial infarction.*
- *Abnormal Q-wave in LIII may be found in pulmonary embolism.*
- *Abnormal Q-wave in LIII and AVf may be found in WPW syndrome (confuses with old inferior myocardial infarction).*

R-WAVE

Characters of normal R-wave:

- Duration <0.01 seconds.
- R-wave is usually small (<1 mm) in V1 and V2. It increases progressively in height in V3–V6 (tall in V5 and V6).

Normal height of R-wave (If R-wave is >25 mm, it is always pathological):

- AVI <13 mm.
- AVf <20 mm.
- V5 and V6 <25 mm.

Abnormalities of R-wave: It may be tall, small, poor progression.

Causes of tall R-wave:

1. LVH (in V5 or V6 >25 mm, AVI >13 mm, aVf >20 mm).
2. In V1, tall R-wave may be as a result of:
 - Normal variant.
 - Right ventricular hypertrophy (RVH).
 - True posterior myocardial infarction.
 - WPW syndrome (type A).
 - Right bundle branch block (RBBB).
 - Dextrocardia.

Causes of small R-wave: Looks like low-voltage tracing.

- Incorrect ECG calibration (standardization).
- Obesity.
- Emphysema.
- Pericardial effusion.
- Hypothyroidism.
- Hypothermia.

R-wave progression: The height of R-wave gradually increases from V1 to V6. This phenomenon is called R-wave progression.

Poor progression of R-wave: Normally, amplitude of R-wave is tall in V5 and V6. In poor R-wave progression, amplitude of R-wave is progressively reduced in V5 and V6. Causes are:

- Anterior or anteroseptal myocardial infarction.
- Left bundle branch block.
- Left ventricular hypertrophy (though R-wave is tall in most cases).
- Dextrocardia.
- Cardiomyopathy.
- Chronic obstructive pulmonary disease (COPD).
- Left-sided pneumothorax.
- Left-sided pleural effusion (massive).
- Marked clockwise rotation.
- Chest electrodes placed incorrectly.
- Deformity of the chest wall.
- Normal variation.

S-WAVE

Characters of normal S-wave:

- Normally, deep in V1 and V2.
- Progressively diminished from V1 to V6.
- In V3, R- and S-waves are almost equal (correspond with the interventricular septum).

QRS COMPLEX

Characters of normal QRS complex:

- QRS complex is predominantly positive in L1, AV1, V5 and V6.
- It is negative in AVr, V1 and V2.
- In V1, S-wave is greater than R-wave and in V5 and V6, R-wave is tall.
- Normal duration of QRS complex is 0.08–0.11 seconds (fewer than three small squares) and height <25 mm.

Abnormalities of QRS complex: It may be of high voltage, low voltage or wide or may change in shape and be variable.

Causes of high-voltage QRS complex:

- Incorrect calibration.
- Thin chest wall.
- Ventricular hypertrophy (right or left or both).
- WPW syndrome.
- True posterior myocardial infarction (in V1 and V2).

Causes of low-voltage QRS complex (<5 mm in LI, LII, LIII and <10 mm in chest leads):

- Incorrect calibration.
- Thick chest wall or obesity.
- Hypothyroidism.
- Pericardial effusion.
- Emphysema.
- Chronic constrictive pericarditis.
- Hypothermia.

Causes of wide QRS complex (>0.12 seconds, three small squares):

- Bundle branch block (LBBB or RBBB).
- Ventricular ectopics.
- Ventricular tachycardia.
- Idioventricular rhythm.
- Ventricular hypertrophy.
- Hyperkalaemia.
- WPW syndrome.
- Pacemaker (looks like LBBB with spike).
- Drugs (quinidine, procainamide, phenothiazine, tricyclic antidepressants).

Causes of changes in the shape of QRS complex:

- RBBB or LBBB (slurred or M-pattern).
- Ventricular tachycardia.
- Ventricular fibrillation.
- Hyperkalaemia.
- WPW syndrome.

Causes of variable QRS complex:

- Multifocal ventricular ectopics.
- Torsades de pointes.
- Ventricular fibrillation.

ST SEGMENT

Characters of normal ST segment:

- Normally, it is in the isoelectric line (lies at the same level of ECG baseline).
- ST elevation is normal up to 1 mm in limb leads and 2 mm in chest leads (mainly V1–V3).
- Normally, ST segment may be depressed, <1 mm.

Abnormalities of ST segment: It may be elevated or depressed.

Causes of ST elevation (>2 mm):

- Recent myocardial infarction (ST elevation with convexity upward).
- Acute pericarditis (ST elevation with concavity upward, chair- or saddle-shaped).
- Prinzmetal angina (ST elevation with tall T-wave).
- Ventricular aneurysm (persistent ST elevation).
- Early repolarization (high takeoff).
- Normal variant in Africans and Asians.
- May be in hyperkalaemia.

Causes of ST depression (below the isoelectric line):

- Acute myocardial ischaemia (horizontal or down slope ST depression with sharp angle ST–T junction).
- Ventricular hypertrophy with strain (ST depression with convexity upward and asymmetric T inversion).
- Digoxin toxicity (sagging of ST depression—such as thumb impression, also called reverse tick).
- Acute true posterior myocardial infarction (in V1 and V2), associated with dominant R-wave and tall upright T-wave.

T-WAVE

Characters of normal T-wave:

- Upright in all leads, except AVr.
- Usually, more than 2 mm in height.
- May be normally inverted in V1 and V2.
- Normally, not more than 5 mm in standard leads and 10 mm in chest leads.
- Minimum one-fourth of R-wave of the same lead.
- Tip of T-wave is smooth (rounded).

Abnormalities of T-wave: It may be inverted, tall, peaked and tented.

Causes of T inversion:

- Myocardial ischaemia and infarction.
- Subendocardial myocardial infarction (non-Q-wave myocardial infarction).
- Ventricular ectopics.
- Ventricular hypertrophy with strain.
- Acute pericarditis.
- Cardiomyopathy.
- Myxoedema.
- Bundle branch block.
- Drugs (digitalis, emetine, phenothiazine).
- Physiological (smoking, anxiety, anorexia, exercise, after meal or glucose).

Causes of tall, peaked T-wave:

- Hyperkalaemia (tall, tented or peaked).
- Hyperacute myocardial infarction (tall T-wave).
- Acute true posterior myocardial infarction (tall T-wave in V1–V2).
- May be normal in some Africans and Asians.

Causes of small T-wave:

- Hypokalaemia.
- Hypothyroidism.
- Pericardial effusion.

U-WAVE

Characters of normal U-wave:

- It is better seen in chest leads (V2–V4).
- Normal amplitude is 1 mm (2 mm in athletes).

Abnormalities of U-wave: It may be inverted or prominent.

Causes of inverted U-wave:

- Ischaemic heart disease.
- LVH with strain (hypertensive heart disease).

Causes of prominent U-wave:

- May be normally present (usually small).
- Hypokalaemia (commonest).
- Bradycardia.
- Ventricular hypertrophy.
- Hyperthyroidism.
- Hypercalcaemia.
- Drugs (phenothiazine, quinidine, digitalis).

N.B. Large U-wave may cause torsades de pointes.

Q–T INTERVAL

Characters of normal Q–T interval:

- Normal Q–T interval is 0.35–0.43 seconds.
- Its duration varies with heart rate, becoming shorter as the heart rate increases and longer as the heart rate decreases.
- It is better seen in AVI (because there is no U-wave).

Abnormalities of Q–T interval: It may be short or long.

Causes of short Q–T interval:

- Digoxin effect.
- Hypercalcaemia.
- Hyperthermia.
- Tachycardia

Causes of long Q–T interval:

- Hypocalcaemia.
- Bradycardia.
- Acute myocarditis.
- Acute myocardial infarction.
- Hypothermia.
- Drug (quinidine, procainamide, flecainide, amiodarone, tricyclic antidepressant, disopyramide, pentamidine).
- Cerebral injury (head injury, intracerebral haemorrhage).
- Hypertrophic cardiomyopathy.
- During sleep.
- Hereditary: Jervell and Lange–Nielsen syndrome, Romano–Ward syndrome.

RHYTHM OF HEART

For rhythm, see the successive R–R interval.

- If the R–R interval is equal, it is called a regular rhythm.
- If the R–R interval is irregular, then it is called an irregular rhythm.

Causes of irregular rhythm

1. Physiological: Sinus arrhythmia.
2. Pathological:
 - Atrial fibrillation.
 - Atrial flutter.
 - Ectopic beat.
 - SA block or sinus arrest.
 - Atrial tachycardia with block.
 - Second-degree heart block.
 - Ventricular fibrillation.

Characters of sinus rhythm: It shows the following five characters:

- P-wave is of sinus origin (means characters of normal P-wave).
- P-waves and QRS complexes are regular (which means P–P and R–R intervals should be constant and identical).
- Constant P-wave configuration in a given lead.
- P–R interval and QRS interval should be within normal limit.
- Rate should be between 60 and 100 beats/min (atrial and ventricular rates are identical).

Q: What is arrhythmia?

A: It is the abnormality in initiation or propagation of cardiac impulse.

CALCULATION OF HEART RATE

Methods vary according to the cardiac rhythm, whether regular or irregular. Heart rate is the number of beats/min.

In the ECG paper:

- 0.04 seconds = one small square.
- 0.2 seconds = five small squares or one large square.
- So, 1 second = 25 small squares or five large squares.
- So, 1 minute = $25 \times 60 = 1500$ small squares or $5 \times 60 = 300$ large squares.

Heart rate is determined in the following way:

1. When the cardiac rhythm is regular:

- Calculate the R–R or P–P interval in small squares or large squares (if the rhythm is sinus, R–R or P–P interval is same).
- If small square is calculated, heart rate is = $1500/(\text{small squares between R–R interval or P–P interval})$.
- If large square is calculated, heart rate is = $300/(\text{large squares between R–R interval or P–P interval})$.

2. When the rhythm is irregular:

- Count the number of R-waves in 30 large squares (it is equivalent to 6 seconds).
- Then simply multiply this by 10 (it becomes rate in 1 minute).

CARDIAC AXIS

Definition: It is the sum of all the depolarization waves as they spread through the ventricles as seen from the front.

Axis determination:

- It can be derived easily from the amplitude of QRS complex in LI, LII and LIII.
- Greatest amplitude of R-wave in LI or LII or LIII indicates the proximity of cardiac axis to that lead.
- Axis lies at 90° to the isoelectric complex, i.e., positive and negative deflections are equal in any of the leads LI, LII, LIII, AVI, AVr and AVf.

Normal axis is between -30° and $+90^\circ$.

Quick and simple way of determination of cardiac axis:

- Positive QRS complex in both LI and LII means axis is normal.
- Positive QRS complex in LI and negative in LIII (tall R-wave in LI and deep S-wave in LIII) mean left-axis deviation.
- Negative QRS complex in LI and positive in LIII (tall R in LIII and deep S in LI) mean right-axis deviation.

Left-axis deviation: When the cardiac axis is between -30° and -90° . Causes are:

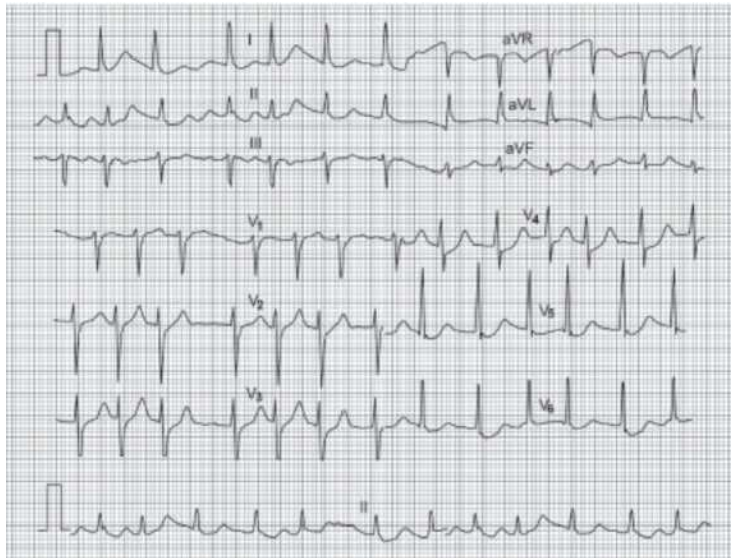
- Normal variant (with advanced age).
- Left ventricular hypertrophy.
- Left anterior hemiblock.
- Left bundle branch block.
- Inferior myocardial infarction.
- T-wave from the apex of the left ventricle.
- WPW syndrome (some).
- Pacing from the apex of the right or left ventricle (endocardial pacing).
- Emphysema.

Right-axis deviation: When the cardiac axis is between $+90^\circ$ and $+180^\circ$. Causes are:

- Normal variant (common in children and young adult).
- Right ventricular hypertrophy (as a result of any cause such as chronic cor pulmonale, pulmonary embolism, congenital heart diseases, i.e., tetralogy of Fallot).
- Anterolateral myocardial infarction (high lateral myocardial infarction).
- Left posterior hemiblock.
- Dextrocardia.
- WPW syndrome (type A).
- Right bundle branch block.
- Epicardial pacing.

SOME COMMON ECG TRACINGS

ECG 01: ATRIAL FIBRILLATION



Atrial fibrillation

Q: Write down three important **abnormal findings** in this ECG.

A: As follows:

- P-wave is absent.
- Rhythm is irregularly irregular (R–R interval is irregular).
- There are fibrillary waves.

Q: What is the **heart rate**?

A: 125 beats/min.

Q: What is your **diagnosis**?

A: Atrial fibrillation.

Q: Write down five important **causes**.

A: As follows:

- Chronic rheumatic heart disease, usually with mitral stenosis.
- Acute myocardial infarction.
- Thyrotoxicosis.
- Hypertension.
- Lone atrial fibrillation.

Q: Write down two important **complications**.

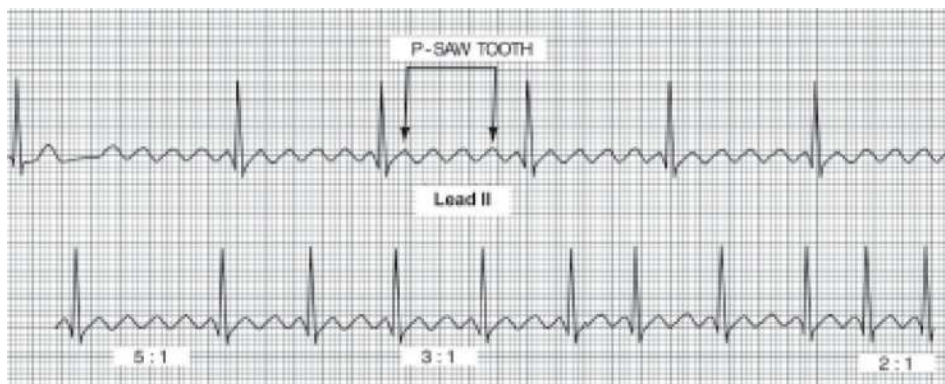
A: As follows:

- Thromboembolism (systemic and pulmonary).
- Heart failure.

Q: If the patient is asymptomatic, mention simple **management**.

A: Low-dose aspirin should be given to prevent thromboembolism.

ECG 02: ATRIAL FLUTTER



Atrial flutter

Q: Write down three important **abnormal findings** in this ECG.

A: As follows:

- P-wave: Saw-toothed appearance (normal P-wave is replaced by flutter or F-wave).
- R-R interval: Irregular.
- Atrial rate: 300 beats/min, ventricular rate is variable (2:1, 3:1 etc.).

Q: What is your **diagnosis**?

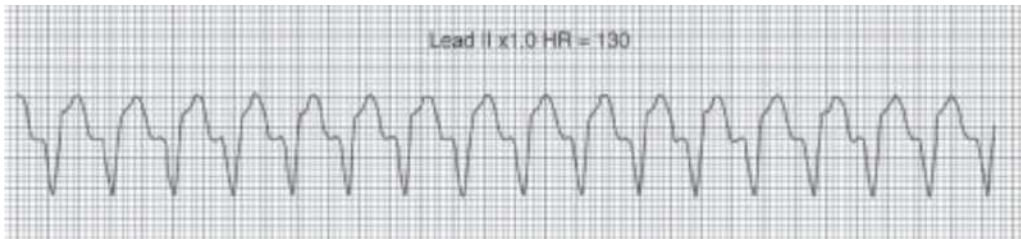
A: Atrial flutter with a variable block.

Q: How to **treat**?

A: As follows:

- To control heart rate: Digoxin, β -blocker or verapamil etc. may be used.
- If no response and the patient has troublesome symptoms: Direct current (DC) cardioversion or atrial overdrive pacing may be done.
- If still no response: Radiofrequency catheter ablation.

ECG 03: VENTRICULAR TACHYCARDIA



Ventricular tachycardia

Q: Write down three important **abnormal findings** in this ECG.

A: As follows:

- P-wave: Absent.
- QRS complex: Broad >0.14 seconds (abnormal or bizarre pattern).
- Ventricular rate: 130 beats/min.

Q: What is your **diagnosis**?

A: Ventricular tachycardia.

Q: Mention two **differential diagnoses**.

A: As follows:

- SVT with RBBB.
- SVT with WPW syndrome.

Q: Mention five **causes**.

A: As follows:

- Acute myocardial infarction.
- Myocarditis.
- Cardiomyopathy.
- Ventricular aneurysm.
- Electrolyte imbalance (mainly hypokalaemia and hypomagnesaemia).

ECG 04: ACUTE MYOCARDIAL INFARCTION

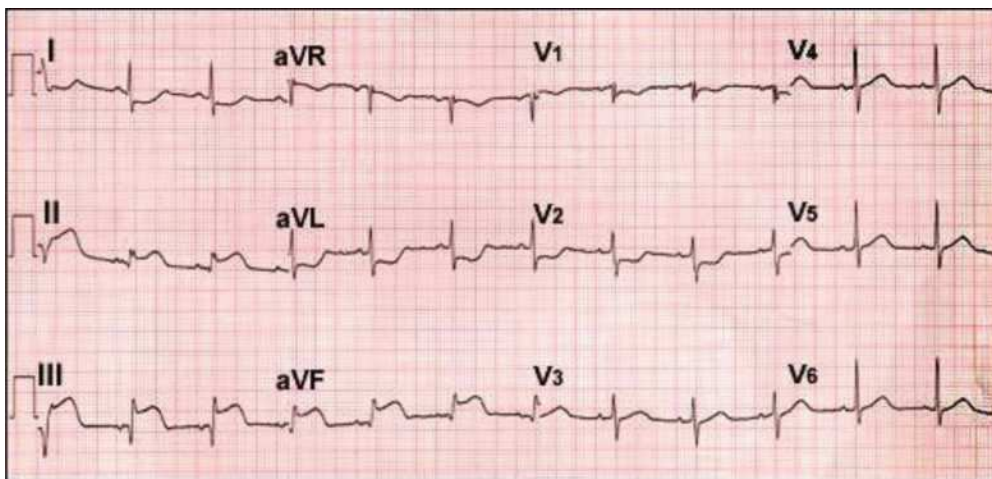


Fig. A: Acute inferior myocardial infarction

Q: Write down two important **abnormal findings** in the ECG shown in Figure A.

A: As follows:

- ST elevation in II, III and AVf.
- ST depression with inverted T-wave in I, AVl and V2.

Q: What is your **diagnosis**?

A: Acute inferior myocardial infarction.

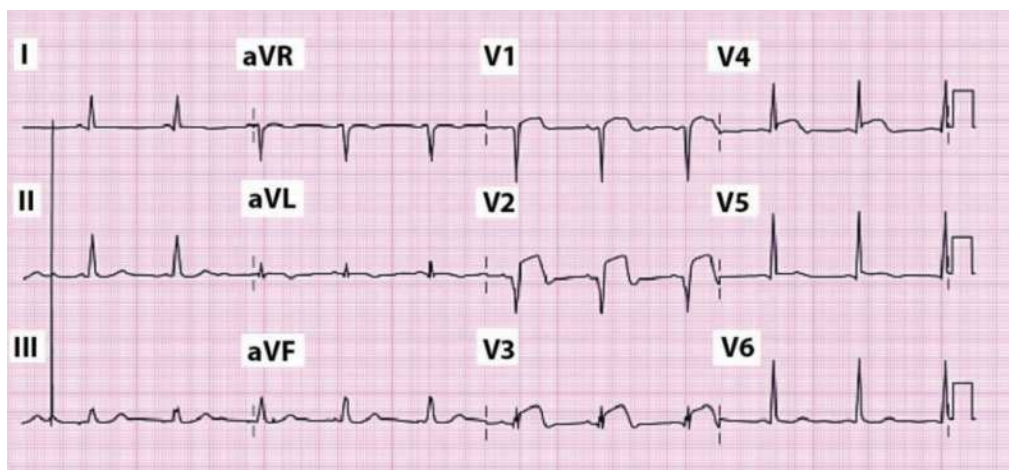


Fig. B: Acute anteroseptal myocardial infarction

Q: Write down two important **abnormal findings** in the ECG shown in Figure B.

A: As follows:

- ST elevation in V1, V2 and V3.
- Pathological Q-waves in V1 and V2.

Q: What is your **diagnosis**?

A: Acute anteroseptal myocardial infarction.

Q: Mention two **investigations**.

A: As follows:

- Serum troponin I.
- Serum CK-MB.

Q: Write down **immediate management plan**.

A: As follows:

- Complete bed rest.
- Oxygen inhalation.
- Tab. chewable aspirin 300 mg orally.
- To relieve pain: Morphine with antiemetic (cyclizine or metoclopramide).
- Thrombolysis (by streptokinase). If possible, primary coronary intervention.

Q: What are the **complications**?

A: As follows:

1. Early complications:
 - Arrhythmia: Ventricular ectopics (more common), ventricular fibrillation, ventricular tachycardia, sinus bradycardia (common in inferior myocardial infarction), sinus tachycardia, atrial fibrillation, heart block.
 - Cardiogenic shock.
 - Cardiac failure (left ventricular failure [LVF], biventricular failure).
 - Acute pericarditis (common on the second or third day).
 - Thromboembolism (systemic and pulmonary).
 - Rupture of the papillary muscle or chordae tendineae resulting in mitral regurgitation.
 - Rupture of interventricular septum, causing ventricular septal defect (VSD).
 - Rupture of the ventricular wall leading to cardiac tamponade.
2. Late complications:
 - Ventricular aneurysm (10%).
 - Postmyocardial infarction syndrome (Dressler syndrome).
 - Frozen shoulder.
 - Postinfarct angina (may occur in up to 50% of patients).

ECG 05: OLD MYOCARDIAL INFARCTION

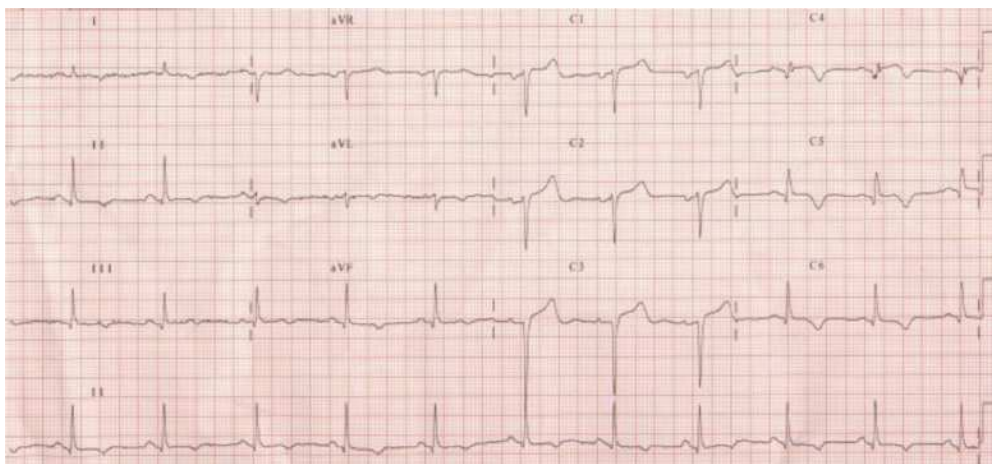


Fig. A: Old anterior myocardial infarction

Q: Write down two important **abnormal findings** in the ECG shown in Figure A.

A: As follows:

- Pathological Q-waves in C1, C2 and C3.
- T inversion in C4, C5 and C6.

Q: What is your **diagnosis**?

A: Old anterior myocardial infarction.

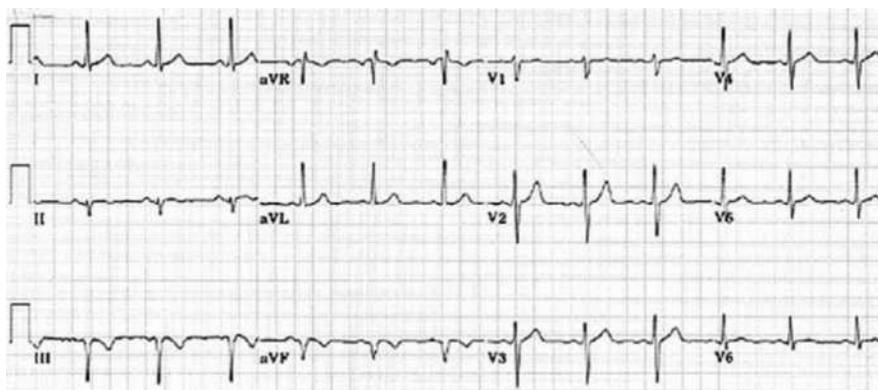


Fig. B: Old inferior myocardial infarction

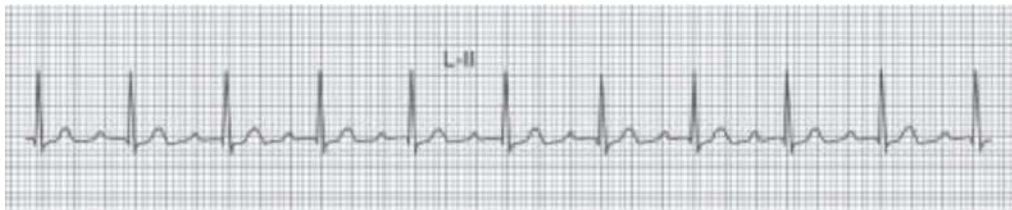
Q: What is the **abnormal finding** in the ECG shown in Figure B?

A: Pathological Q-wave in II, III and AVf.

Q: What is your **diagnosis**?

A: Old inferior myocardial infarction.

ECG 06: FIRST-DEGREE AV BLOCK



First-degree AV block

Q: What is the abnormal **finding** in this ECG?

A: P-R interval is prolonged >0.22 seconds (normal 0.12–0.20 seconds).

Q: What is your diagnosis?

A: First-degree AV block.

Q: Mention four **causes**?

A: As follows:

- Digoxin toxicity.
- Acute myocardial infarction (common in inferior myocardial infarction).
- Acute rheumatic carditis.
- Hyperkalaemia.

ECG 07: SECOND-DEGREE AV BLOCK (MOBITZ TYPE I)



Second-degree AV block (Mobitz type I)

Q: Write down two important **abnormal findings** in this ECG.

A: As follows:

- Progressive lengthening of P–R interval, followed by an absent QRS complex (one P is not followed by a QRS complex).
- R–R interval: Irregular (progressive shortening of R–R interval until block occurs).

Q: What is your **diagnosis**?

A: Second-degree AV block, Mobitz type I (Wenckebach phenomenon).

Q: Mention three **causes**?

A: As follows:

- Physiological: Athlete, during rest, sleep (as a result of increased vagal tone).
- Drugs: Digoxin toxicity.
- Acute myocardial infarction (commonly inferior myocardial infarction).

Q: Where is the **lesion**?

A: The block is in the higher area of AV node (proximal to bundle of His).

Q: What is the **prognosis**?

A: Good prognosis.

ECG 08: SECOND-DEGREE AV BLOCK (MOBITZ TYPE II)



Second-degree AV block (Mobitz type II)

Q: Write down three important **findings** in this ECG.

A: As follows:

- P–R interval is constant (also P–P interval constant).
- QRS complex: Wide.
- Alternate P-wave is conducted.

Q: What is your **diagnosis**?

A: Mobitz type II second-degree AV block with 2:1 conduction.

Q: What are the **complications**?

A: As follows:

- Complete heart block.
- Stokes–Adams syndrome.
- Heart failure.

Q: Where is the **lesion**?

A: Disease of the His–Purkinje system.

Q: Mention the most **likely cause**.

A: Common in acute anterior myocardial infarction.

Q: How to **treat**?

A: As follows:

1. When associated with acute inferior myocardial infarction:
 - If asymptomatic—close monitoring and follow-up.
 - If symptomatic—Inj. atropine 0.6 mg i.v. If no response, temporary pacemaker. The majority will resolve in 7–10 days.
2. If associated with acute anterior myocardial infarction—temporary pacing, followed by permanent pacemaker (because complete heart block may develop).

ECG 09: COMPLETE HEART BLOCK



Complete heart block

Q: Write down three important **abnormal findings** in this ECG.

A: As follows:

- Atrial rate is 60/min, P–P interval is constant.
- Ventricular rate is 35/min.
- There is no relationship between P-wave and QRS complex

Q: What is your **diagnosis**?

A: Complete heart block.

Q: Write down three findings you expect in **CVS (Cardiovascular system) examination**.

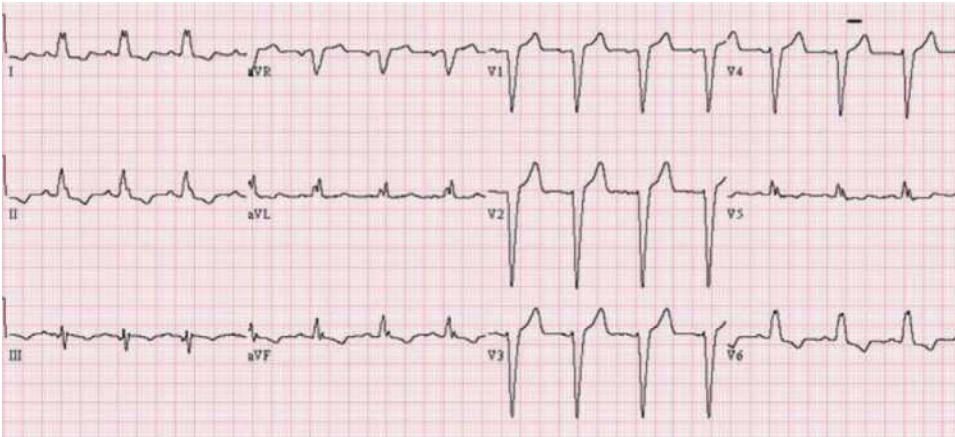
A: As follows:

- Pulse: Bradycardia (<40/min), high volume, does not increase by exercise.
- Cannon waves (large a-wave) in the neck vein.
- Variable intensity of the first heart sound.

Q: What is the **management**?

A: Permanent pacemaker.

ECG 10: LEFT BUNDLE BRANCH BLOCK



Left bundle branch block

Q: Write down two important **abnormal findings** in this ECG.

A: As follows:

- Wide QRS complex in all leads.
- RSR' pattern in I, aVL, aVF, V5 and V6.

Q: What is your **diagnosis**?

A: Left bundle branch block.

Q: What finding might you get on **auscultation**?

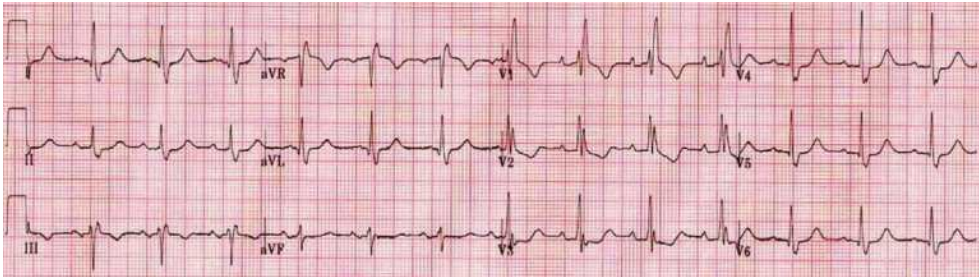
A: Reverse splitting of the second heart sound.

Q: Mention four **causes**.

A: As follows:

- Severe coronary artery disease.
- Acute myocardial infarction.
- Cardiomyopathy.
- Aortic valve disease (stenosis or regurgitation).

ECG 11: RIGHT BUNDLE BRANCH BLOCK



Right bundle branch block

Q: Write down two important **abnormal findings** in this ECG.

A: As follows:

- Wide QRS complex in all leads.
- RSR' pattern in V1, V2 and V3.

Q: What is your **diagnosis**?

A: Right bundle branch block.

Q: Mention three **causes**.

A: As follows:

- Normal variant.
- Coronary artery disease (acute myocardial infarction).
- Atrial septal defect (ASD).
- Cardiomyopathy.

ECG 12: LEFT VENTRICULAR HYPERTROPHY

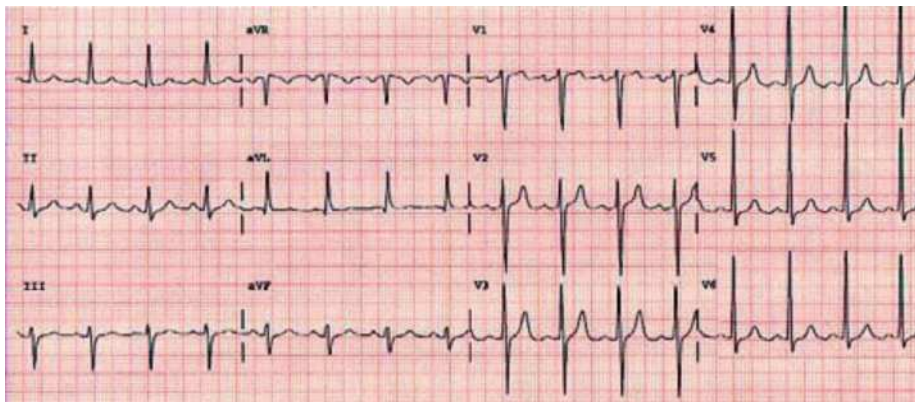


Fig. A: Left ventricular hypertrophy

Q: Write down two **abnormal findings** in the ECG shown in Figure A.

A: As follows:

- S-wave in V1 + R-wave in V6 = 39 mm (criteria: S-wave in V1 + R-wave in V6 >35 mm).
- Left-axis deviation.

Q: What is your **diagnosis**?

A: Left ventricular hypertrophy.

Q: Mention one finding in the examination of **precordium**.

A: Apex beat is heaving in nature.

Q: Mention one **investigation** to confirm the diagnosis.

A: Echocardiography (M-mode).

Q: Mention five **causes**.

A: As follows:

- Systemic hypertension.
- Aortic stenosis.
- Coarctation of aorta.
- Hypertrophic cardiomyopathy.
- Ventricular septal defect.

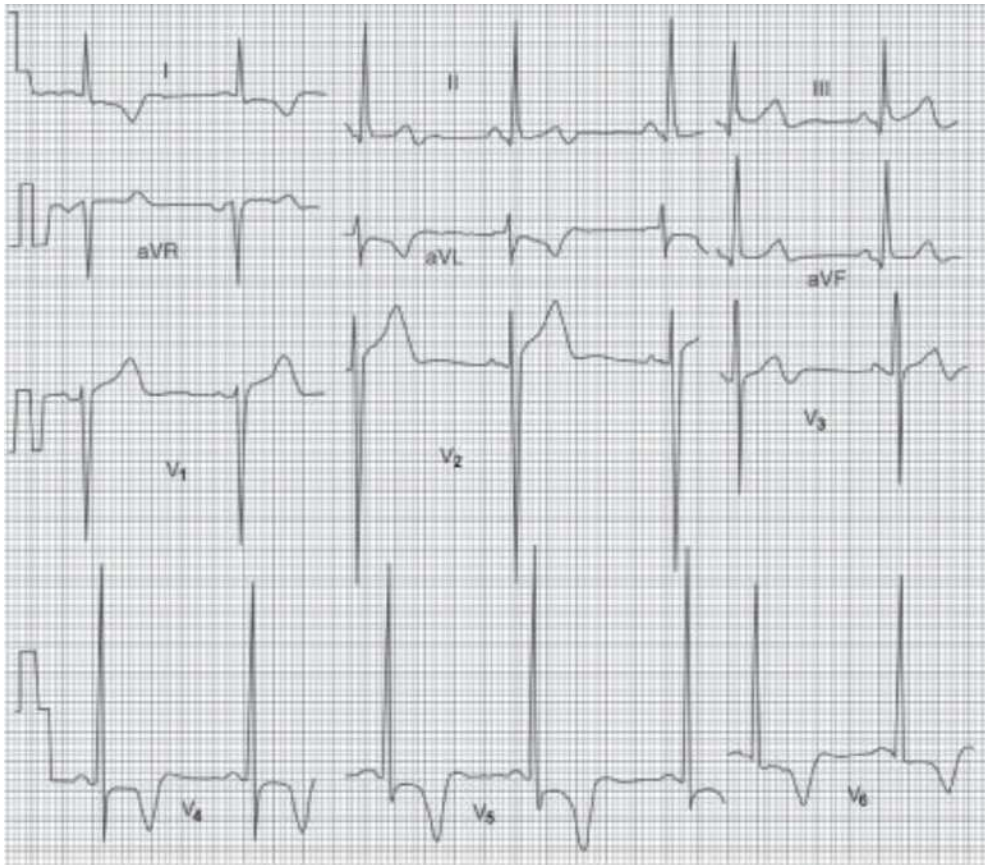


Fig. B: Left ventricular hypertrophy with strain

Q: Write down two **abnormal findings** in the ECG shown in Figure B.

A: As follows:

- S-wave in V1 + R-wave in V6 = 51 mm (criteria: S-wave in V1 + R-wave in V6 >35 mm).
- ST-wave depression and T-wave inversion in I, aVL, V4–V6.

Q: What is your **diagnosis**?

A: Left ventricular hypertrophy with strain.

Q: What are the **differential diagnoses**?

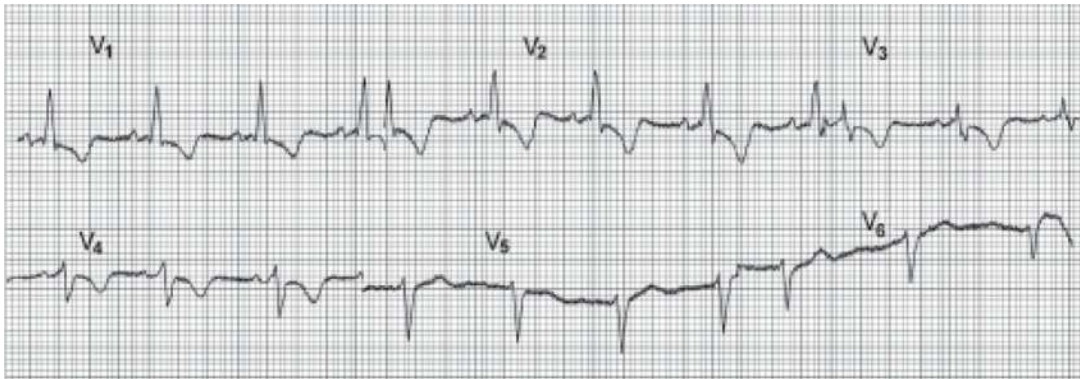
A: As follows:

- Hypertrophic cardiomyopathy.
- Subendocardial myocardial infarction.

Q: Mention one **investigation** to confirm the diagnosis.

A: Echocardiography (two-dimensional [2D] or M-mode).

ECG 13: RIGHT VENTRICULAR HYPERTROPHY



Right ventricular hypertrophy with strain

Q: Write down two **abnormal findings** in this ECG.

A: As follows:

- R-wave in V1 = 10 mm (criteria: tall R-wave in V1 >7 mm).
- ST-wave depression and T-wave inversion (in V1 and V2).

Q: What is your **diagnosis**?

A: Right ventricular hypertrophy with strain.

Q: Mention four **clinical findings**.

A: As follows:

- Palpable P2.
- Left parasternal heave.
- Epigastric pulsation.
- Loud P2 on auscultation.

Q: Mention one **investigation** to confirm the diagnosis.

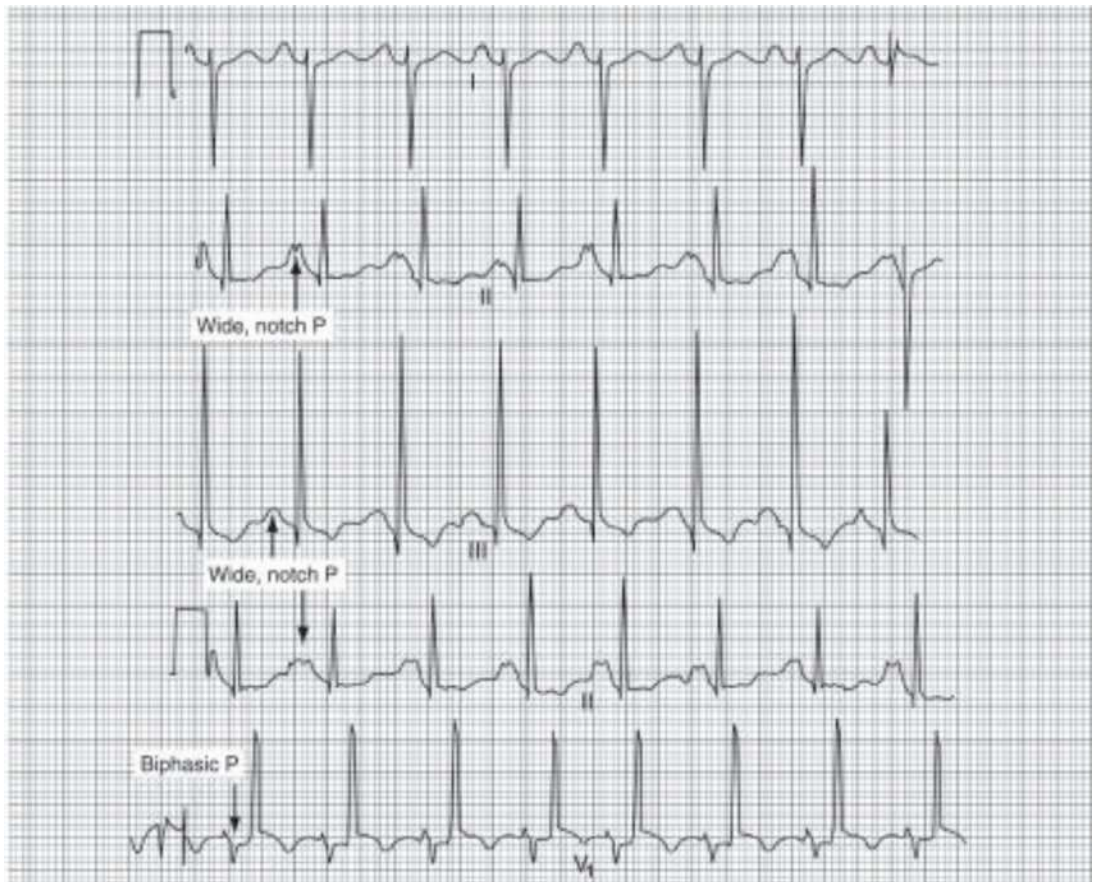
A: Echocardiogram (2D and M-mode).

Q: Mention five **causes**.

A: As follows:

- Chronic cor pulmonale.
- Mitral stenosis with pulmonary hypertension.
- Primary pulmonary hypertension.
- Pulmonary stenosis.
- Eisenmenger syndrome.
- Tetralogy of Fallot.

ECG 14: P MITRALE



P mitrale

Q: Write down three **abnormal findings** in this ECG.

A: As follows:

- P-wave is wide (> 0.12 seconds) in LII and III.
- P-wave is notched (or bifid) in LII (called P mitrale).
- P-wave in V1 is biphasic with prominent deep negative deflection (> 1 -mm depth) and small initial positive deflection.

Q: What is your **diagnosis**?

A: P mitrale.

Q: What does it **indicate**?

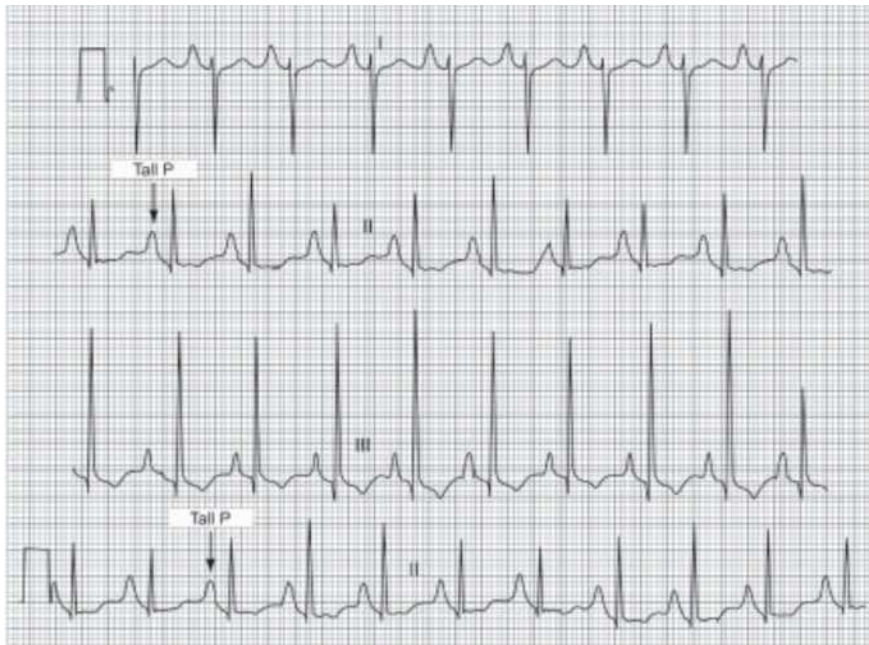
A: It indicates left atrial hypertrophy or enlargement.

Q: Mention two **causes** of such an ECG finding.

A: As follows:

- Mitral stenosis (commonest).
- Mitral regurgitation.

ECG 15: P PULMONALE



P pulmonale

Q: What is the **abnormal finding** in this ECG?

A: P-wave is tall (>2.5 mm) in LI, II and III (P pulmonale).

Q: What is your **diagnosis**?

A: P pulmonale.

Q: What does it **indicate**?

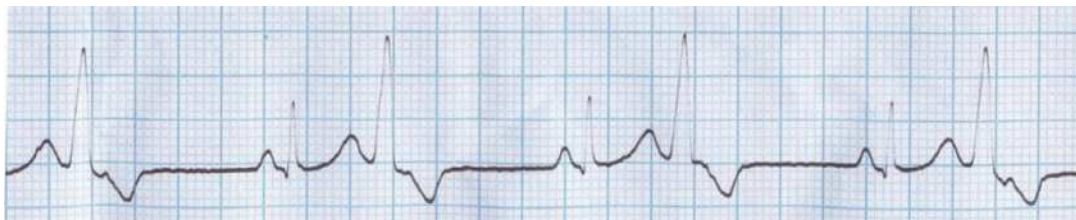
A: It indicates right atrial hypertrophy or enlargement.

Q: Mention five **causes** of such an ECG finding.

A: As follows:

- COPD with chronic cor pulmonale (commonest).
- Atrial septal defect.
- Tricuspid regurgitation or stenosis.
- Pulmonary stenosis.
- Pulmonary hypertension (as a result of any cause).

ECG 16: PULSUS BIGEMINY



Pulsus bigeminy

Q: What is the **abnormal finding** in this ECG?

A: Every normal beat is followed by a ventricular ectopic beat.

Q: What is your **diagnosis**?

A: Ventricular bigeminy.

Q: Mention five **causes**.

A: As follows:

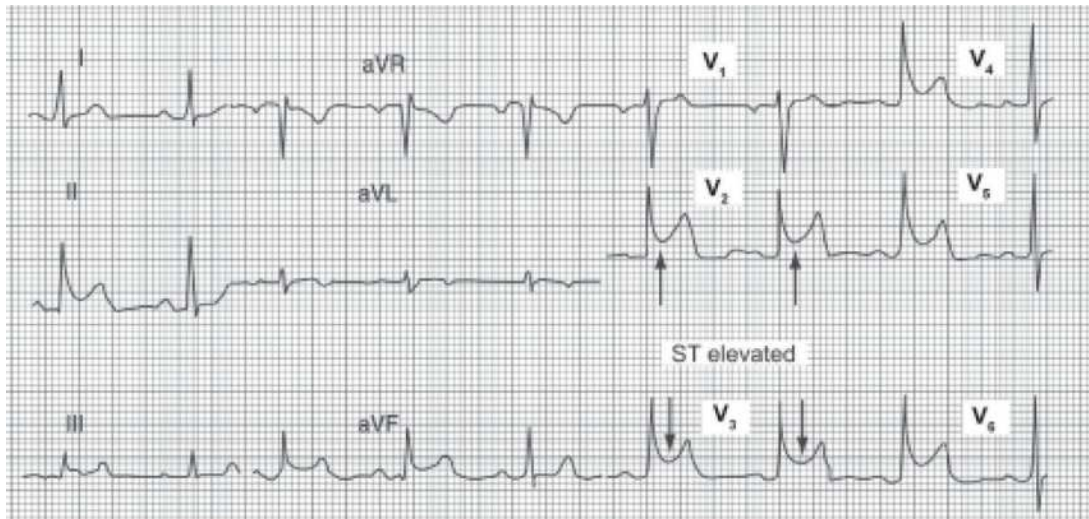
- Digoxin toxicity.
- Myocarditis.
- Cardiomyopathy.
- After acute myocardial infarction.
- Electrolyte imbalance (hypokalaemia).
- Hypoxaemia.

Q: How to **treat**?

A: As follows:

- Any offending drug should be stopped.
- Correction of electrolytes, especially hypokalaemia, hyperkalaemia and hypomagnesaemia.
- Treatment of primary cause or any organic heart disease.
- If asymptomatic: No other treatment.
- If symptomatic: β -Blocker (antiarrhythmic drugs should be avoided, as they may worsen the prognosis).

ECG 17: ACUTE PERICARDITIS



Acute pericarditis

Q: Mention the **abnormal finding**.

A: ST is elevated with upward concavity in LII, AVf, V2, V3, V4, V5 and V6.

Q: What is your **diagnosis**?

A: Acute pericarditis.

Q: Mention one **clinical finding**.

A: Pericardial rub.

Q: Mention five **causes**.

A: As follows:

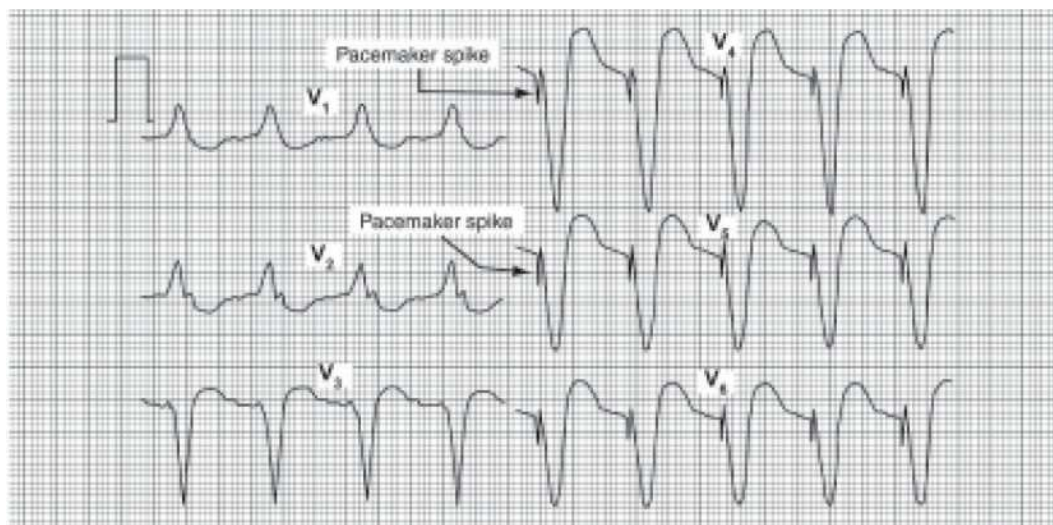
- Following acute myocardial infarction (usually on the second or third day).
- Infective: Viral (coxsackievirus B, echovirus) common cause. Others are bacterial (*Staphylococcus aureus*, *Haemophilus influenzae*), tuberculous pericarditis and fungal (histoplasmosis, coccidioidomycosis).
- Acute rheumatic fever.
- Acute renal failure.
- Malignancy (from carcinoma of bronchus, breast, lymphoma, leukaemia).
- Collagen disease (systemic lupus erythematosus [SLE], scleroderma).

Q: How to **treat**?

A: As follows:

- To relieve pain—nonsteroidal anti-inflammatory drug (NSAID) (indomethacin or ibuprofen or aspirin).
- In severe or recurrent case, corticosteroids should be given.
- If no response to steroid, azathioprine or colchicine may be given.
- If recurrence with no response to medical treatment, pericardiectomy may be done.
- Treatment of primary cause—antibiotic, if bacterial infection. Anti-Koch, if tuberculosis is suspected.

ECG 18: PACEMAKER



Ventricular pacemaker

Q: Mention two **abnormal findings**.

A: As follows:

- There is a spike, followed by a QRS complex.
- QRS complex is wide (looks like LBBB).

Q: What is your **diagnosis**?

A: Ventricular pacemaker.

Q: Mention two **absolute indications**.

A: As follows:

- Sick sinus syndrome.
- Stokes–Adams syndrome.

ECG 19: SINUS TACHYCARDIA



Sinus tachycardia

Q: Write down three important **findings** in this ECG.

A: As follows:

- Heart rate: 110/min.
- Rhythm: Normal.
- P-wave, QRS complex and T-wave: Normal.

Q: What is your **diagnosis**?

A: Sinus tachycardia.

Q: Write down five important **causes**.

A: As follows:

- Physiological: Anxiety, emotion, exercise, pain, pregnancy.
- Anaemia.
- Fever.
- Thyrotoxicosis.
- Shock (except vasovagal attack in which bradycardia is present).
- Heart failure.

N.B. Other causes are:

- *Chronic constrictive pericarditis.*
- *Acute anterior myocardial infarction (bradycardia is common in acute inferior myocardial infarction).*
- *Drugs (salbutamol, atropine, adrenaline, isoprenaline, ephedrine, propantheline, thyroxine).*

ECG 20: SINUS BRADYCARDIA



Sinus bradycardia

Q: Write down three important **findings** in this ECG.

A: As follows:

- Heart rate: 50/min.
- Rhythm: Regular.
- P-wave, QRS complex and T-wave: Normal.

Q: What is your **diagnosis**?

A: Sinus bradycardia.

Q: Write down five important **causes**.

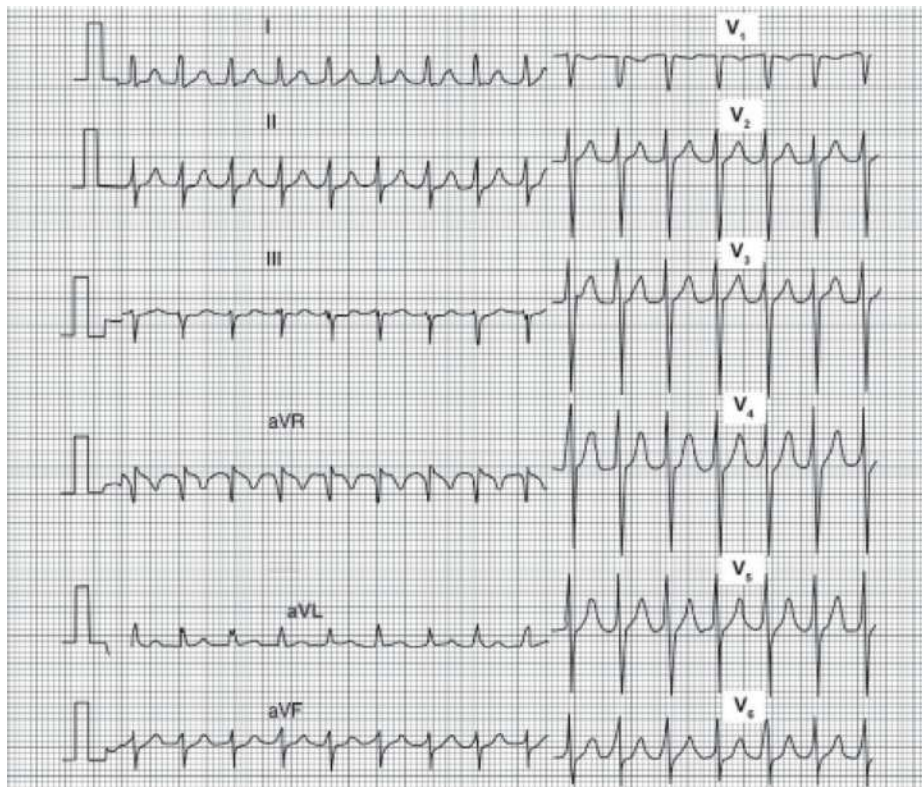
A: As follows:

- Physiological: In athletes, during sleep.
- Hypothyroidism.
- Hypothermia.
- Raised intracranial pressure (as a result of inhibitory effect on sympathetic outflow).
- Drugs (digoxin, β -blockers, verapamil).

N.B. Other causes are:

- Acute inferior myocardial infarction.
- Obstructive jaundice (as a result of deposition of bilirubin in the conducting system).
- Electrolyte imbalance (hypokalaemia).
- Neurally mediated syndromes as a result of a reflex (Bezold–Jarisch), which causes bradycardia and reflex peripheral vasodilatation. These are carotid sinus syndrome, neurocardiogenic (vasovagal) syncope (syndrome), which presents as syncope or presyncope.

ECG 21: SUPRAVENTRICULAR TACHYCARDIA



Supraventricular tachycardia

Q: Write down four important **findings** in this ECG.

A: As follows:

- Heart rate: 140/min.
- Rhythm: Regular.
- P-wave: Absent.
- QRS complex: Narrow.

Q: What is your **diagnosis**?

A: Supraventricular tachycardia.

Q: Write down five important **causes**.

A: As follows:

- Physiological: Anxiety, tea, coffee, alcohol.
- Thyrotoxicosis.
- Ischaemic heart disease.
- WPW syndrome.
- Digitalis toxicity.

Q: What is the complication?

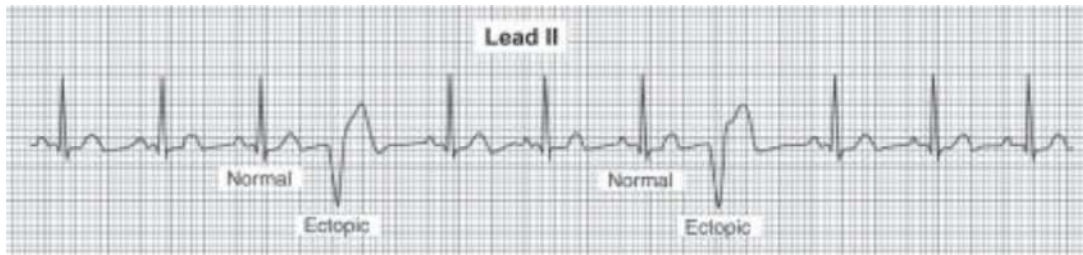
A: Heart failure may occur as a result of reduction of stroke volume (rapid heart rate causes short diastolic filling time with low diastolic filling).

Q: How to treat?

A: As follows:

1. Rest and reassurance.
2. Carotid sinus massage or Valsalva manoeuvre. It acts by increasing the vagal tone.
3. If no response:
 - Adenosine—3 mg i.v. over 2 seconds. If no response in 1–2 minutes, then 6 mg i.v. If still no response in 1–2 minutes, then 12 mg.
 - Or verapamil 10 mg i.v. slowly over 5–10 minutes (verapamil should be avoided if QRS complex >0.12 seconds or a history of WPW syndrome or if the patient is taking β -blocker).
4. Other drugs: β -Blocker, disopyramide or digoxin may be used.
5. If the patient is haemodynamically unstable (hypotension, pulmonary oedema), then DC shock should be given.
6. If the attack is frequent or disabling: Prophylactic oral therapy with β -blocker, verapamil, disopyramide or digoxin may be given.
7. In WPW syndrome: Transvenous radiofrequency catheter ablation is the treatment of choice.
8. If there is no response: Antitachycardial pacing is done (overdrive atrial pacing).

ECG 22: VENTRICULAR PREMATURE BEAT



Ventricular premature beat

Q: Write down three important findings in this ECG.

A: There are two ventricular premature beats with the following characteristics:

- P: Absent.
- QRS complex: Wide >0.12 seconds (three small squares).
- T: Opposite to major deflection.

Q: What is your diagnosis?

A: Ventricular premature (ectopic) beats.

Q: Write down five important causes.

A: As follows:

- Normally in young adults, as well as in anxiety, excess caffeine, alcohol.
- Acute myocardial infarction.
- Myocarditis.
- Cardiomyopathy.
- Electrolyte imbalance (especially hypokalaemia).
- Digoxin toxicity.
- Mitral valve prolapse.

Q: What are the types?

A: As follows:

- *Unifocal*: Similar configuration of ectopics in all leads; it originates from a single ectopic ventricular focus.
- *Multifocal*: Variable configuration of ectopics in the same lead; ectopics originate from different foci of the ventricle.
- *Interpolated ventricular ectopics*: It means when ventricular ectopics occur between two normal sinus beats without a compensatory pause.

Other Types

- *Couplet*: Two ventricular ectopics in a row, multifocal.
- *Triplet*: Three ventricular ectopics in a row (runs of ectopic, three or more ventricular ectopics in a row, may be taken as ventricular tachycardia).
- *Ventricular bigeminy*: Every one normal beat, followed by ventricular ectopic.

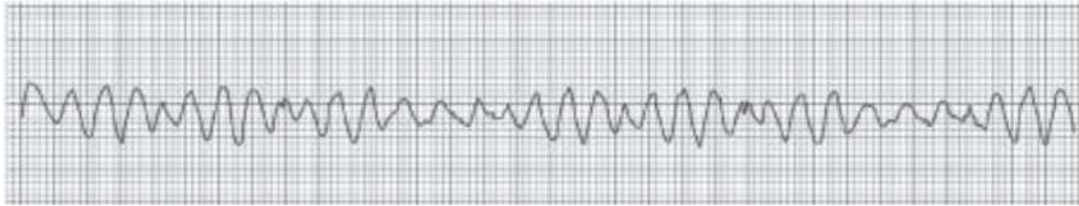
- *Ventricular trigeminy*: Every two normal beats, followed by ventricular ectopic.
- *Ventricular quadrigeminy*: Every three normal beats, followed by ventricular ectopic.
- *Grouped ventricular ectopics*: Two to five consecutive ventricular ectopics.

Q: How to treat?

A: As follows:

- In the absence of any heart disease and in asymptomatic case: No treatment is necessary. β -Blocker may be used.
- With organic heart disease: Treatment of the primary cause.

ECG 23: VENTRICULAR FIBRILLATION



Ventricular fibrillation

Q: What is the **finding** in this ECG.

A: QRS complex: Chaotic, wide, bizarre, irregular.

Q: What is your **diagnosis**?

A: Ventricular fibrillation.

Q: Write down five important **causes**.

A: As follows:

- Acute myocardial infarction.
- Electrolyte imbalance (hypokalaemia, hypomagnesaemia).
- Electrocution.
- Drowning.
- Drug overdose (digitalis, adrenaline, isoprenaline).

Q: Mention six clinical **signs** in this patient.

A: As follows:

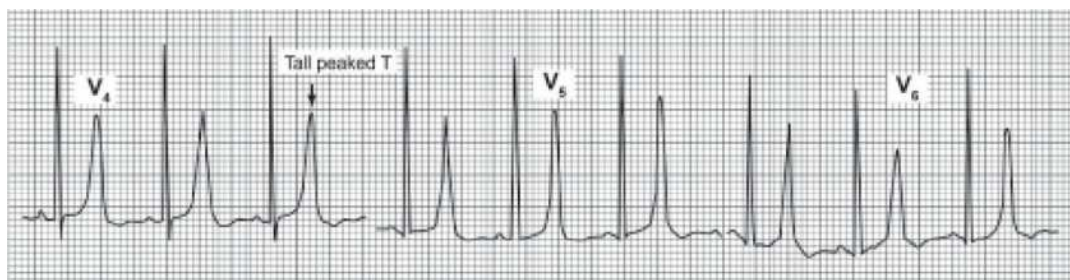
- Pulse: Absent.
- Blood pressure (BP): Not recordable.
- Respiration: Ceases or absent.
- Patient: Unconscious.
- Pupil: Dilated, less or no reaction to light.
- Heart sounds: Absent.

Q: How to **treat**?

A: As follows:

- Immediate defibrillation: 200 Joules. If no response, another shock with 200 Joules is given. If still no response, another shock with 360 Joules is given.
- If three shocks unsuccessful: Adrenaline is given intravenously, followed by cardiopulmonary resuscitation.
- If defibrillator is not available, cardiopulmonary resuscitation should be given.
- The patient who survives ventricular fibrillation in the absence of identifiable cause is at a high risk of sudden death. This case is treated with implantable cardioverter defibrillator.

ECG 24: HYPERKALAEMIA



Hyperkalaemia

Q: Write down two important **findings** in this ECG.

A: As follows:

- T-wave: Tall, peaked and tented.
- P-wave: Wide and small.

N.B. Other probable findings are (not seen in this ECG):

- P-R interval: Prolonged.
- QRS complex: Wide, slurred and bizarre.

Q: What is your **diagnosis**?

A: Hyperkalaemia.

Q: Write down four important **causes**.

A: As follows:

1. High potassium intake.
2. Renal diseases:
 - Acute and chronic renal failure.
 - Impaired tubular secretion of K^+ (renal lupus, amyloidosis, transplanted kidney).
3. Endocrine diseases:
 - Addison disease.
 - Diabetic ketoacidosis.
 - Primary hypoaldosteronism.
4. Drugs: Potassium-sparing diuretics (spironolactone, amiloride, triamterene), angiotensin-converting-enzyme (ACE) inhibitor, NSAID, cyclosporine.

Q: Write four clinical **features**.

A: As follows:

- Muscular weakness; it may be severe, causing flaccid paralysis, loss of tendon jerk.
- Paralytic ileus (abdomen may be distended).
- Tingling around the lip or finger.
- Sudden death as a result of cardiac arrest or arrhythmia.

Q: How to treat?**A:** As follows:

- Withdrawal of potassium, potassium-containing food and offending drug.
- Injection 10% calcium gluconate 10–20 mL i.v. slowly over 10 minutes.
- Injection 50 mL of 50% glucose i.v. + Inj. insulin 10 units.
- Correction of acidosis: By soda bicarb (1.26%) 500 mL i.v. 6–8 hourly (until serum HCO_3 is normal).
- Treatment of primary causes.
- In some cases, exchange resins (calcium resonium 15–30 g orally).
- If all fail: Haemodialysis or peritoneal dialysis.

PICTURES

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PICTURES

16

'Diagnosis is not the end, but the beginning of practice'
— Martin H. Fischer

PICTURE 01: INFECTED SCABIES



Q: Write down the **finding** shown in this picture.

A: Multiple vesicular and pustular lesions in interdigital and dorsal surface of both hands.

Q: What is your **diagnosis**?

A: Infected scabies.

Q: What is the causative **organism**?

A: *Sarcoptes scabiei*.

Q: What are the common **sites**?

A: As follows:

- Interdigital space.
- Antecubital fossa.

- Axilla.
- Nipple.
- Umbilicus.
- Scrotum.

Q: What are the **differential** diagnoses?

A: As follows:

- Papular urticaria.
- Atopic dermatitis.
- Dermatitis herpetiformis.
- Pediculosis corporis.

Q: Write down two important **complications** of this clinical condition.

A: Secondary bacterial infection and poststreptococcal glomerulonephritis.

Q: Write down the **treatment**.

A: As follows:

1. General measures: Control of infection by antibiotics; for itching—antihistamine, washing of cloths and bed sheet, simultaneous treatment of other family members.
2. Specific treatment:
 - Local: 5% permethrin cream. Other drugs are 1% γ -benzene hexachloride, 25% benzyl benzoate, 10% precipitated sulphur in white petroleum.
 - Systemic: Ivermectin orally when local treatment fails.

PICTURE 02: PURPURA



Q: What are the **findings** seen in the photograph?

A: Multiple purpuric spots of variable sizes and shapes in both lower limbs.

Q: Mention six **differential** diagnoses.

A: As follows:

- Drug rash.
- Idiopathic thrombocytopenic purpura (ITP).
- Henoch–Schonlein purpura.
- Dengue haemorrhagic fever.
- Aplastic anaemia.
- Meningococcal septicaemia.

Q: Mention six **important investigations** for this patient.

A: As follows:

- Complete blood count (CBC) with peripheral blood film (PBF).
- Anti-dengue antibody.
- Blood for culture and sensitivity (C/S).
- Coagulation profile: Prothrombin time, activated partial thromboplastin time (APTT).
- Screening for disseminated intravascular coagulation (DIC): Fibrin degradation products (FDP), D-dimer.
- Bone marrow study.

PICTURE 03: RHEUMATOID ARTHRITIS



Q: What are the **abnormalities** in this photograph?

A: As follows:

- Swan-neck deformity of fingers.
- Z-deformity of thumb.
- Ulnar deviation of hands.
- Flexion deformity of metacarpophalangeal joints.

Q: What is the **diagnosis**?

A: Rheumatoid arthritis (RA).

Q: Mention five important **investigations**.

A: As follows:

- CBC, erythrocyte sedimentation rate (ESR).
- C-reactive protein (CRP).
- RA and Rose–Waler (RW) tests.
- Anticyclic citrullinated peptide (anti-CCP) antibody.
- X-ray of both hands.

Q: Mention the modalities of **treatment**.

A: As follows:

1. To relieve pain: Nonsteroidal anti-inflammatory drug (NSAID).
2. Suppression of activity and progression of disease: Disease-modifying antirheumatic drug (DMRD).
3. Physiotherapy.
4. Orthopaedic measures.

PICTURE 04: ARTHRITIS MUTILANS

Q: What are the **findings**?

A: Complete disorganization and deformity involving all the joints of both hands.

Q: What is the likely **diagnosis**?

A: Arthritis mutilans in RA.

Q: What specific **measures** can be done in such a case?

A: Orthopaedic measures such as reconstructive surgery along with treatment of RA.

PICTURE 05: GRAVES DISEASE



Q: Write down four important **findings** in this picture.

A: As follows:

- Bilateral exophthalmos.
- Diffuse goitre.
- Anxious look.
- Wasting.

Q: What is your **diagnosis**?

A: Graves disease.

Q: What **other finding** you should look for in this case?

A: Dermopathy.

Q: Mention three important **questions** you will ask the patient.

A: As follows:

- Preference to hot or cold.
- Increased appetite and weight loss.
- Excessive sweating.

Q: Write down three important **clinical findings**.

A: As follows:

- Palm: Warm and sweaty.
- Tremor of the outstretched hand.
- Tachycardia.

Q: Write down the most important **investigation** to diagnose the case.

A: As follows:

- Free tri-iodothyronine (FT₃), free thyroxine (FT₄), thyroid-stimulating hormone (TSH).
- Radioiodine uptake test.
- Thyroid scanning.
- Ultrasonogram of the neck.
- TSH receptor antibody.

Q: What is the **natural history** of this disease?

A: The patient may have hyperthyroidism, followed by euthyroidism and then hypothyroidism.

PICTURE 06: PSORIASIS



Picture A

Q: Write down the important **findings** in Picture A.

A: Multiple, well-circumscribed erythematous plaques with silvery white scales on both lower limbs.

Q: What is your **diagnosis**?

A: Psoriasis.



Picture B

Q: Write down the important **findings** in Picture B.

A: Multiple, well-circumscribed erythematous plaques with silvery white scales on the back.

Q: What is your **diagnosis**?

A: Psoriasis.

Q: What are the **differential** diagnoses?

A: As follows:

- Dermatomyositis.
- Lichen planus.
- Seborrhoeic dermatitis.
- Secondary syphilis.

Q: Mention two important **physical signs** that should be seen in this patient.

A: Auspitz sign and Koebner phenomenon.

Q: Mention one **investigation** to confirm your diagnosis.

A: Skin biopsy.

Q: How to **treat**?

A: As follows:

1. General measures: Explanation and reassurance, avoid trauma.
2. Specific therapy:
 - Local therapy: Crude tar 3%–5%, dithranol, calcipotriol, ultraviolet radiation (UVR).
 - Systemic therapy: PUVA (psoralen plus UV ray), retinoid, methotrexate (MTX).
3. Other therapy: anti-TNF- α (infliximab, etanercept).

PICTURE 07: SYSTEMIC LUPUS ERYTHEMATOSUS



Q: Write down the important **findings** in this picture.

A: Multiple skin rashes on the face along the butterfly distribution.

Q: What is your **diagnosis**?

A: Systemic lupus erythematosus (SLE).

Q: Mention four **differential** diagnoses.

A: As follows:

- Dermatomyositis.
- Drug rash.
- Post-kala-azar dermal leishmaniasis (PKDL).
- Lepromatous leprosy.

Q: Mention two **investigations** to confirm your diagnosis.

A: As follows:

- Antinuclear antibody (ANA).
- Anti-ds-DNA (Anti-double-stranded deoxyribonucleic acid).

Q: Name five **drugs** that may cause this disease.

A: As follows:

- Hydralazine.
- Procainamide.
- Anticonvulsant: Carbamazepine, phenytoin.
- Penicillamine.
- Oral contraceptive pill.
- Isoniazid (INH).

PICTURE 08: ERYTHEMA MULTIFORME**Picture A**

Q: Write down the important **findings** in these pictures.

A: Multiple erythematous vesicular lesions on both forearms and erythematous lesions involving both palms.

Q: What is your **diagnosis**?

A: Erythema multiforme.

**Picture B**

Q: What is the **pathognomonic lesion** in this disease?

A: Target lesion.

Q: What are the **differential diagnoses**?

A: As follows:

- Drug reaction.
- SLE.
- Dermatitis herpetiformis.
- Dermatomyositis.

Q: Mention two **causes**.

A: As follows:

- Infection: Herpes simplex type 1, *Mycoplasma pneumoniae*.
- Drugs: Sulphonamide, carbamazepine, thioacetazone.

Q: What **investigations** should be done?

A: As follows:

- CBC, ESR.
- Antibody to herpes simplex virus and *Mycoplasma pneumoniae*.
- Chest X-ray.

PICTURE 09: LEPROSY



Q: Write down the important **findings** in this picture.

A: As follows:

- Multiple erythematous nodules of variable sizes and shapes on the forehead, ear and face.
- Multiple pigmented and depigmented areas over the same area.

Q: What is your **diagnosis**?

A: Lepromatous leprosy.

Q: What is the causative **organism**?

A: *Mycobacterium leprae*.

Q: Mention four **differential** diagnoses.

A: As follows:

- PKDL.
- Sarcoidosis.
- Drug rash.
- Dermatomyositis.

Q: What investigations should be done to **confirm** the diagnosis?

A: Skin-slit smear for acid-fast bacilli (AFB) staining.

Q: What drugs are used to **treat** the case?

A: As follows:

- Dapsone.
- Rifampicin.
- Clofazimine.

PICTURE 10: STEVENS–JOHNSON SYNDROME



Picture A

Q: Write down the important **findings** in Picture A.

A: Multiple erythematous lesions and ulcerations involving the skin and mucous membrane of the face, lips and oral cavity.

Q: What is your **diagnosis**?

A: Stevens–Johnson syndrome.



Picture B

Q: Write down the important **findings** in Picture B.

A: As follows:

- Desquamation and ulceration of skin of the scrotum.
- Multiple, sharply demarcated pigmented lesions over the lower abdomen and upper thighs.

Q: What is your **diagnosis**?

A: Stevens–Johnson syndrome.

Q: Mention three **causes**.

A: As follows:

- Drug reaction: Sulphonamide, carbamazepine, thiacetazone.
- Infection by herpes simplex virus, *Mycoplasma pneumoniae*.
- Idiopathic.

PICTURE 11: RING WORM



Q: Write down the important **findings** in this picture.

A: Multiple circular lesions on both antecubital fossae, showing central healing with peripherally active lesion.

Q: What is your **diagnosis**?

A: Ring worm infection (tinea corporis).

Q: How to **confirm**?

A: Microscopic examination of skin scrapping in KOH preparation.

Q: What are the causative **organisms**?

A: As follows:

- *Trichophyton*.
- *Epidermophyton*.
- *Microsporum*.

Q: How to **treat**?

A: As follows:

- Maintain hygiene.
- Local antifungal agents such as miconazole.
- Systemic antifungal agents such as fluconazole.

PICTURE 12: SUBCONJUNCTIVAL HAEMORRHAGE

Q: Write down the important **findings** in this picture.

A: Subconjunctival haemorrhage in both eyes.

Q: Mention three **causes**?

A: As follows:

- Trauma.
- Dengue fever.
- Bleeding disorder.

Q: How to **treat**?

A: As follows:

- Local: Antibiotic eyedrops, analgesics for pain.
- Treatment of the cause.

PICTURE 13: BELL PALSY



Picture A

Q: Write down the important **findings** in Picture A.

A: As follows:

- Difficulty in closing the right eye (mention if Bell phenomenon is also seen).
- Mouth is deviated to the left on showing the teeth.
- No wrinkling of the forehead on the right side.
- Facial asymmetry.
- Nasolabial fold less prominent on the right side.

Q: What is your **diagnosis**?

A: Right-sided Bell palsy.



Picture B

Q: Write down the important **findings** in Picture B.

A: As follows:

- Bell's phenomenon on closing the right eye.
- Nasolabial fold less prominent on the right side.

Q: What is your **diagnosis**?

A: Right-sided Bell palsy.

Q: What are the **causes** if it was bilateral?

A: As follows:

- Guillain–Barré syndrome (GBS).
- Sarcoidosis.
- Lyme disease.

Q: How to **treat**?

A: As follows:

- Prednisolone 40–60 mg daily plus acyclovir for 7 days.
- Artificial tear.
- Physiotherapy.

PICTURE 14: RAMSAY HUNT SYNDROME



Q: What is the **finding** in this picture?

A: Vesicular rash on the external ear with pus in external auditory meatus.

Q: This patient also has right-sided facial palsy. What is the **diagnosis**?

A: Ramsay Hunt syndrome.

Q: What is the **cause**?

A: Varicella zoster virus.

PICTURE 15: GOITROUS MYXOEDEMA

Q: What are the abnormal **findings** in this picture?

A: As follows:

- Diffuse goitre.
- Puffy face.

Q: What is the likely **diagnosis**?

A: Goitrous myxoedema.

Q: Mention two **causes**.

A: As follows:

- Hashimoto thyroiditis.
- Iodine-deficiency goitre.

Q: Write three **clinical features**.

A: As follows:

- Intolerance to cold.
- Weight gain.
- Increased sleepiness.

Q: Write one important bedside physical **sign**.

A: Slow relaxation of ankle jerk.

Q: If the patient complains of **tingling and numbness** of fingers, what is the likely diagnosis?

A: Carpal tunnel syndrome.

Q: Mention three **investigations** to confirm your diagnosis.

A: As follows:

- FT₃, FT₄, TSH.
- Antithyroglobulin and antiperoxidase antibody.
- Ultrasonogram of the neck.

Q: How to **treat**?

A: Lifelong thyroxine therapy.

PICTURE 16: GONORRHOEA

Q: Write down the important **finding** in this picture.

A: Purulent urethral discharge.

Q: What is your **diagnosis**?

A: Gonorrhoea.

Q: What **investigations** should be done?

A: Urethral swab for Gram stain and C/S.

Q: How to **treat**?

A: Antibiotics such as ceftriaxone, ciprofloxacin etc.

PICTURE 17: HIRSUTISM



Picture A

Q: What is the **finding** in Picture A?

A: Increased facial hair in an elderly female patient.

Q: What is the **diagnosis**?

A: Hirsutism.

Q: Mention three **causes**?

A: As follows:

- Androgen-secreting ovarian tumour.
- Adrenal carcinoma.
- Idiopathic.



Picture B

Q: Mention three **findings** in Picture B.

A: As follows:

- Increased facial hair in a young female patient.
- Puffy face with flushing.
- Facial acne.

Q: What is the **likely diagnosis** in this patient?

A: Cushing syndrome.

Q: Mention three **differential diagnoses**.

A: As follows:

- Polycystic ovary syndrome (PCOS).
- Androgen-secreting ovarian tumour.
- Late-onset congenital adrenal hyperplasia.

PICTURE 18: OSTEOARTHRISIS



Q: What are the **findings** in this picture?

A: Nodular swelling on the distal interphalangeal joint of the right little and ring fingers.

Q: What is the likely **diagnosis**?

A: Osteoarthritis.

Q: What is the **lesion** called?

A: Heberden node.

PICTURE 19: PERIPHERAL VASCULAR DISEASE

Q: What is the **finding** in this picture?

A: Blackening and necrosis of the index fingers of both hands and the middle and little fingers of the left hand.

Q: What is the **diagnosis**?

A: Peripheral vascular disease, most likely Buerger disease.

Q: Mention three **differential diagnoses**.

A: As follows:

- Atherosclerosis.
- Raynaud disease.
- Systemic sclerosis.

PICTURE 20: HYPOPITUITARISM



Q: What are the findings in this picture of a 45-year-old man?

A: As follows:

- Short stature.
- Bilateral gynaecomastia.

Q: What is the likely diagnosis?

A: Hypopituitarism.

Q: Mention one investigation.

A: Magnetic resonance imaging (MRI) of the pituitary fossa.

PICTURE 21: HERPES ZOSTER**Picture A**

Q: What is the **finding** in Picture A?

A: Multiple vesicular lesions over the left shoulder, left upper chest and upper part of the left arm along left C4 dermatome.

Q: What is the **diagnosis**?

A: Herpes zoster.

Q: How to **treat**?

A: Acyclovir and local skin care (such as antiseptic cream, regular cleaning)

Q: Mention one **complication**.

A: Post-herpetic neuralgia.

**Picture B**

Q: What is the **finding** in Picture B?

A: Ulcerated lesions over the right half of the forehead, around the right eye and over the right maxillary region.

Q: What is the **diagnosis**?

A: Herpes zoster ophthalmicus.

Q: What is the causative **organism**?

A: Varicella zoster virus.

Q: How to **treat**?

A: As follows:

- Acyclovir.
- Care of the eye.

PICTURE 22: OBSTRUCTIVE JAUNDICE

Q: Write two **findings** in this picture?

A: As follows:

- Deep jaundice.
- Cachexia.

Q: What is the likely **diagnosis**?

A: Obstructive jaundice, most likely as a result of carcinoma of the head of pancreas.

Q: Mention three **investigations**.

A: As follows:

- Liver function tests: Serum bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, prothrombin time.
- Ultrasonogram of the hepatobiliary system and the pancreas.
- Computed tomographic (CT) scan of the abdomen.

PICTURE 23: WEGENER GRANULOMATOSIS



Q: What are the **findings**?

A: Swelling on the forehead, left upper eyelid and nasal bridge.

Q: This patient presented with recurrent rhinitis with cough. What is the likely **diagnosis**?

A: Wegener granulomatosis.

Q: Mention three **investigations**.

A: As follows:

- X-ray of chest PA view.
- Cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA).
- Biopsy from the nasal crust or the affected part.

Q: What are the **differential diagnoses**?

A: As follows:

- Sarcoidosis.
- Lymphoma.
- Tuberculosis.
- Midline granuloma (idiopathic).
- Fungal: Histoplasmosis.
- Lymphomatoid granulomatosis.
- Rhinoscleroma.

PICTURE 24: XANTHELASMA

Q: What is the **finding** in this picture?

A: Xanthelasma.

Q: What does it **indicate**?

A: Dyslipidaemia.

Q: What **investigation** should be done?

A: Fasting lipid profile.

Q: Mention three **causes**.

A: As follows:

- Primary biliary cirrhosis.
- Nephrotic syndrome.
- Familial hypercholesterolaemia.

PICTURE 25: BAKER CYST



Q: What is the **finding** in this picture?

A: Swelling on the back of the right knee.

Q: What is the likely **diagnosis**?

A: Baker cyst.

Q: Mention three **causes**.

A: As follows:

- Rheumatoid arthritis.
- Osteoarthrosis.
- Congenital.

Q: Mention one **complication**.

A: Rupture of Baker cyst.

Q: Mention one **investigation**.

A: Ultrasonogram of the knee joint.

PICTURE 26: PECTUS CARINATUM

Q: What are the **findings** in this picture?

A: As follows:

- Pectus carinatum (pigeon chest).
- Kyphosis.

Q: What are the **causes**?

A: As follows:

- Congenital.
- Rickets.
- Marfan syndrome.
- Homocystinuria.
- Repeated respiratory infection in childhood.
- Bronchial asthma since childhood.
- Osteogenesis imperfecta.

PICTURE 27: CORNEAL ARCUS



Q: Write down the abnormal **finding** in the eyes of this 75-year-old patient.

A: Whitish opaque ring around the corneal margin.

Q: What is it **called**?

A: Corneal arcus.

Q: Mention two **causes**.

A: As follows:

- Arcus senilis.
- Dyslipidaemia.

PICTURE 28: ACROMEGALY



Q: What is the abnormal **finding**? What is it **called**?

A: Protrusion of the lower jaw. It is called prognathism.

Q: What is the likely **diagnosis**?

A: Acromegaly.

Q: Mention four other **clinical findings** in this patient.

A: As follows:

- Enlarged skull, body and limbs.
- Hands are large, spade-like.
- Thick skin with skin tags.
- Bitemporal hemianopia.

Q: What **investigations** should be done to confirm your diagnosis?

A: As follows:

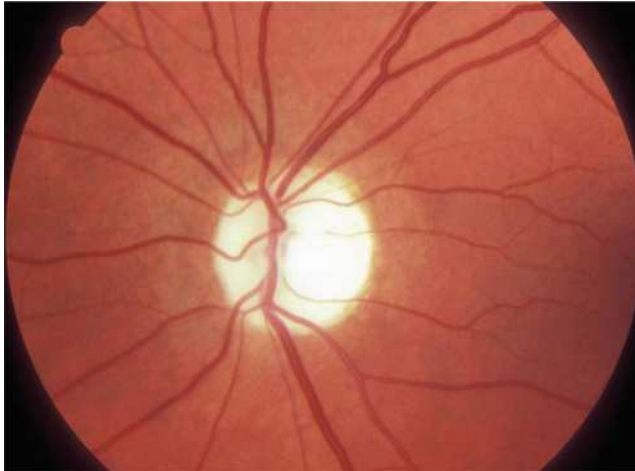
- X-ray of the skull, hands.
- MRI of the brain.
- Growth hormone measurement with simultaneous oral glucose tolerance test (OGTT).
- Insulin-like growth factor 1 (IGF1).

Q: What are the modalities of **treatment**?

A: As follows:

- Medical treatment: Octreotide.
- Surgical: Transphenoidal removal of pituitary tumour.
- Radiotherapy.

PICTURE 29: PRIMARY OPTIC ATROPHY



Q: What are the **findings**?

A: As follows:

- The disc is pale with a clear margin.
- There is reduction in the number of capillaries in the disc.

Q: What is the **diagnosis**?

A: Primary optic atrophy.

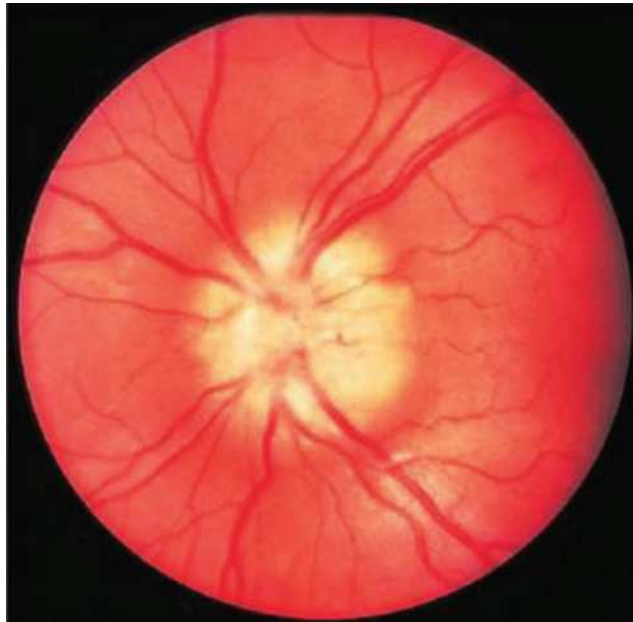
Q: What is the **mechanism**?

A: Degeneration of optic nerve fibres.

Q: Mention four **causes**.

A: As follows:

- Intracranial space-occupying lesion.
- Secondary to optic neuritis.
- Glaucoma.
- Optic nerve compression by tumour or aneurysm.

PICTURE 30: PAPILLOEDEMA

Q: What is the **finding** in this picture?

A: There is blurring of the disc margin with fullness of the optic disc.

Q: What is the **diagnosis**?

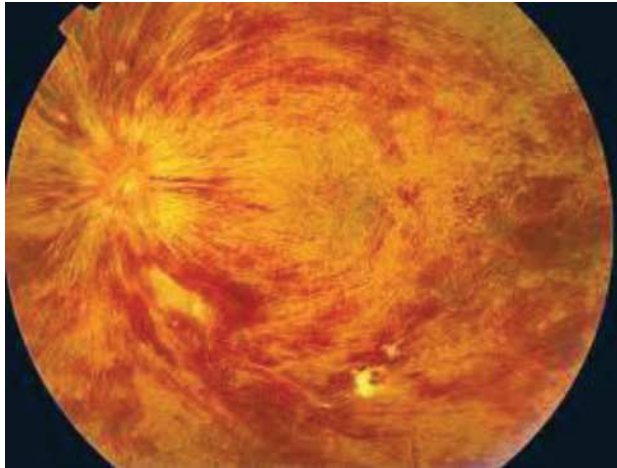
A: Papilloedema.

Q: Mention two **causes**?

A: As follows:

- Raised intracranial pressure as a result of the space-occupying lesion (e.g., tumour, abscess, haematoma).
- Benign intracranial hypertension.

PICTURE 31: CENTRAL RETINAL VEIN OCCLUSION



Q: What are the **findings**?

A: As follows:

- Multiple scattered haemorrhages over the whole retina, giving a stormy sunset appearance.
- Veins are dilated and tortuous.
- Few soft exudates and papilloedema are present.

Q: What is the **diagnosis**?

A: Central retinal vein occlusion.

Q: Mention five **causes**.

A: As follows:

- Hypertension.
- Atherosclerosis.
- Diabetes mellitus.
- Hyperviscosity syndrome.
- Hyperlipidaemia.

Q: Mention three serious **complications**.

A: As follows:

- Glaucoma (rubeotic).
- Optic atrophy.
- Permanent loss of vision.

Q: What **investigations** should be done?

A: As follows:

- CBC.
- Blood sugar.
- Plasma viscosity.
- Plasma protein electrophoresis.
- Lipid profile.
- Bone marrow (to exclude multiple myeloma).

INSTRUMENTS

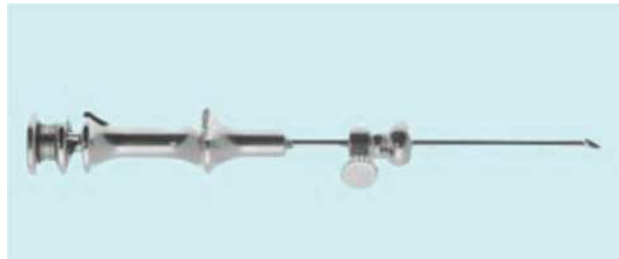
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‘When you no longer know what headache, heartache or stomachache means without cistern punctures, electrocardiograms and six x-ray plates, you are slipping’.
—Martin H. Fischer

INSTRUMENT 01: BONE MARROW ASPIRATION NEEDLE



Q: What is this **instrument**?

A: Bone marrow aspiration needle (also called sternal puncture needle).

Q: What are its **parts**?

A: Three parts:

- Trocar.
- Cannula.
- Adjustable guard.

Q: Mention the **sites** of use.

A: As follows:

- Manubrium sterna or body of the sternum.
- Posterior superior iliac crest.
- Other sites: Upper part of the medial surface of tibia just below the tibial tuberosity in children.
Rarely, spinous process of lumbar vertebrae.

Q: How can you **confirm** that the needle has **reached** the cavity?

A: When the needle is in the bone marrow cavity, there is sudden loss of resistance and marrow material is seen at the tip of the trocar.

Q: What are the indications of bone marrow study?**A:** As follows:

- Aplastic anaemia.
- Megaloblastic anaemia.
- Macrocytic anaemia as a result of any cause.
- Multiple myeloma.
- Leukaemia.
- Myelofibrosis.
- Pancytopenia as a result of any cause.
- Idiopathic thrombocytopenic purpura (ITP).
- Kala-azar to see Leishman–Donovan (LD) bodies.

Q: What are its contraindications?**A:** As follows:

- Local infection or sepsis.
- Bleeding disorders such as haemophilia.
- Platelet count <40,000/cmm.

Q: What are the causes of dry or blood tap?**A:** As follows:

- Faulty technique.
- Myelosclerosis or myelofibrosis.
- Marrow hypoplasia.
- Sometimes in marrow hyperplasia or leukaemia, if the marrow is heavily packed with cells.
- Tumour infiltration, e.g., lymphoma, secondary malignancy.

Q: What are its complications?**A:** As follows:

- Suction pain.
- Vasovagal attack as a result of fear or pain.
- Bleeding and localized haematoma.
- Injury to the underlying structure as a result of overpenetration.
- Infection, e.g., osteomyelitis.

Q: What is trephine biopsy?**A:** Trephine biopsy shows histological section that contains bony trabeculae, haemopoietic tissue, fat cells and blood vessels.**Q: What are the indications of trephine biopsy?****A:** As follows:

- Dry or blood tap.
- In aplastic anaemia: For better assessment of cellularity.
- Myelofibrosis or myelosclerosis.
- If bone marrow aspiration fails to establish a diagnosis.
- Diagnosis and staging of lymphoma.
- Secondary deposits.

INSTRUMENT 02: LUMBAR PUNCTURE NEEDLE



Q: What is this **instrument**?

A: Lumbar puncture (LP) needle.

Q: What are its **parts**?

A: As follows:

- Cannula with a cap.
- Trocar.

Q: What are its **uses**?

A: As follows:

1. Diagnostic:
 - Meningitis.
 - Encephalitis.
 - Subarachnoid haemorrhage.
 - Guillain–Barré syndrome.
 - Multiple sclerosis.
2. Therapeutic:
 - Intrathecal methotrexate in acute lymphoblastic leukaemia (ALL).
 - Spinal anaesthesia.
 - Removal of cerebrospinal fluid (CSF) in benign intracranial hypertension.

Q: Mention the anatomical **sites** of using this instrument. Why these sites are chosen?

A: In the space between L3 and L4 or L4 and L5. These sites are chosen because the spinal cord is absent at these spaces. So, there is no chance of injury.

N.B. The line between the highest points of both iliac crests runs through the spinous process of the fourth lumbar vertebra.

Q: What are its **contraindications**?

A: As follows:

- Raised intracranial pressure (clinically detected if there is papilloedema).
- Localized infection.
- Bleeding disorder (e.g., haemophilia, Christmas disease etc.).

Q: What **clinical examination** would you do before LP? Why?

A: Ophthalmoscopy to see papilloedema, which indicates raised intracranial pressure. If LP is done in such a case, there may be herniation of cerebellar tonsil through the foramen magnum and may compress the vital centre in medulla oblongata and cause sudden death.

Q: What are its complications?**A:** As follows:

- Post-LP headache.
- Infection (causing meningitis, arachnoiditis).
- Bleeding.
- Herniation of cerebellar tonsil.
- Persistent CSF leaking.
- Injury to local structures such as intervertebral disc, vessels, nerves etc.

Q: What is post-LP headache? How to manage it?**A:** Headache usually occurs if LP is done in normal intracranial tension. It results from low intracranial tension as a result of withdrawal of CSF, which causes traction on the meningeal blood vessel, resulting in headache.

Treatment is as follows:

- Increased fluid intake.
- The patient should lie flat for 8–24 hours.
- Foot end should be raised and the head pillow should be removed.
- Analgesics.

Q: How much CSF is drawn during LP?**A:** For diagnostic purpose, 5–8 mL; for therapeutic purpose, 10–20 mL is drawn.**Q: What are the causes of dry tap?****A:** As follows:

- Faulty technique.
- Spinal subarachnoid block (e.g., as a result of meningioma, neurofibroma, epidural abscess etc.).

Q: What should be seen in CSF?**A:** As follows:

- Pressure.
- Physical character: Colour (clear, purulent, haemorrhagic, straw). If the fluid is kept for 8–12 hours, there may be a cobweb appearance. Also xanthochromia may be seen.
- Biochemistry: Protein, sugar, chloride.
- Cytology: Cell count, differential count.
- Microbiology: Gram stain, culture and sensitivity, acid-fast bacilli (AFB).
- Serology: Viral serology, Venereal Disease Research Laboratory (VDRL), *Cryptococcus* etc.
- Polymerase chain reaction (PCR) done in herpes simplex virus, *Mycobacterium tuberculosis* etc.
- Oligoclonal band on protein electrophoresis.

Q: What are the characteristics of normal CSF?**A:** As follows:

- Amount: 100–150 mL.
- Pressure: 50–150 mm H₂O on lying; 150–250 mm H₂O on sitting.
- Colour: Clear.
- Protein: 20–40 mg/dL.
- Glucose: 50–80 mg/dL (two-thirds of blood glucose level).
- Chloride: 720–750 mg/dL.
- Cytology: 0–5 cells/cmm (all are lymphocytes).

Q: What are the causes of raised intracranial pressure?**A:** As follows:

- Meningitis.
- Encephalitis.
- Intracranial space-occupying lesion.
- Benign intracranial hypertension.
- Intracranial haemorrhage.
- Intracranial sinus thrombosis.
- Hydrocephalus.
- Hypertensive encephalopathy.

Q: What are the causes of decreased intracranial pressure?**A:** As follows:

- Dehydration.
- Spinal block.

Q: What are the different colours of CSF?**A:** As follows:

- Clear: Normal, viral encephalitis.
- Haemorrhagic: As a result of blood (see below).
- Yellow: Xanthochromia (see below).
- Straw: Tuberculosis (cobweb is formed when kept overnight).
- Turbid or cloudy: Pyogenic meningitis.

Q: What are the causes of blood-stained CSF?**A:** As follows:

- Trauma.
- Subarachnoid haemorrhage.
- Blood leakage from cerebral tumour
- Coagulation disorder (haemophilia, Christmas disease, excess use of anticoagulants etc.).

Q: How can you differentiate traumatic bleeding from subarachnoid haemorrhage?**A:** Usually, three samples are taken.

Points	Traumatic Bleeding	Subarachnoid Bleeding
Colour	Initially red but becomes faint, red or clear in later samples	All the samples are uniformly red
Clot	Present	Absent
Xanthochromia	Absent	Present when kept for sometime

Q: What are the causes of xanthochromia (yellow colour)?**A:** As follows:

- Old subarachnoid haemorrhage.
- Froin syndrome.
- Deep jaundice.

Q: What are the causes of **increased protein** in CSF?

A: As follows:

- Guillain–Barré syndrome.
- Spinal block.
- Acoustic neuroma.
- Froin syndrome.
- Tubercular meningitis.
- Pyogenic meningitis.
- Neurosyphilis (rarely).
- Carcinomatosis.

N.B. Protein level is very high in the first four indications.

Q: What are the causes of **raised γ -globulin** in CSF?

A: As follows:

- Multiple sclerosis.
- Neurofibromatosis.
- Connective tissue disorder.

Q: What are the causes of **decreased sugar** in CSF?

A: As follows:

- Tubercular meningitis.
- Pyogenic meningitis.
- Hypoglycaemia.
- Carcinomatous meningitis.

Q: What are the causes of **raised sugar** in CSF?

A: Hyperglycaemia (diabetes mellitus).

Q: What are the causes of **increased lymphocyte** count in CSF?

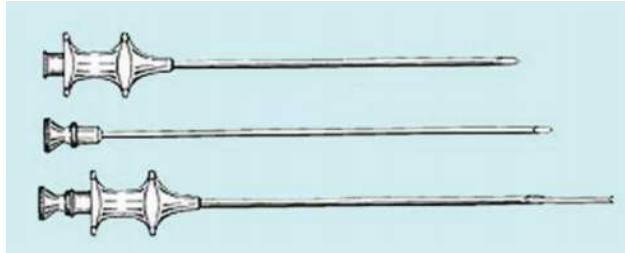
A: As follows:

- Tubercular meningitis.
- Viral meningitis or encephalitis.
- Neurosyphilis.

Q: What is the cause of **increased neutrophil** count in CSF?

A: Pyogenic meningitis.

INSTRUMENT 03: LIVER BIOPSY NEEDLE



Q: What is this **instrument**?

A: Vim Silverman liver biopsy needle.

Q: What are its **parts**?

A: As follows:

- Cannula.
- Trocar.
- Split needle.

Q: Name different **types of instruments** for liver biopsy.

A: As follows:

- Vim Silverman needle (commonly used).
- Menghini needle.
- Trucut needle.

Q: What are the **indications** of liver biopsy?

A: As follows:

- Chronic liver disease (CLD) (cirrhosis of liver, chronic hepatitis).
- Space-occupying lesions:
 - Hepatic carcinoma.
 - Secondary deposits in the liver.
- Metabolic disorder:
 - Haemochromatosis.
 - Wilson disease.
- Infiltrative disease:
 - Sarcoidosis.
 - Lymphoma.
- Amyloidosis.
- Storage diseases (e.g., glycogen storage disease).
- Unexplained hepatomegaly.

Q: What are the **contraindications** of liver biopsy?

A: As follows:

- Bleeding disorders, e.g., haemophilia, Christmas disease.
 - Hydatid cyst.
- Passive venous congestion of liver.
- Extrahepatic cholestasis or biliary obstruction.
- Severe jaundice.
- Hepatic encephalopathy (the patient may fall into coma).

Q: What **prerequisites** should be taken before doing liver biopsy?

A: As follows:

- The patient should be cooperative; consent should be taken.
- To be excluded: Biliary obstruction, marked ascites, severe anaemia and high bilirubin.
- Prothrombin time should not be >4 of control.
- Platelet count should not be $<100,000/\text{cmm}$.
- Blood grouping and cross-matching.

Q: How to be sure that the **needle is in the liver**?

A: After introducing the needle, the patient is asked to take deep breath in and out. The needle will move with respiration.

Q: What are the **causes of failure** of liver biopsy?

A: As follows:

- Faulty technique.
- Severe fibrosis of liver.

Q: How to do the **follow-up** after biopsy?

A: As follows:

- The patient should be in complete bed rest for 24 hours.
- Regular monitoring of pulse, blood pressure (BP).
- Blood should be kept ready for transfusion.

Q: What are the **complications**?

A: As follows:

- Bleeding.
- Shock.
- Secondary infection.
- Injury to colon and other viscera.
- Pleurisy.
- Pneumothorax.
- Biliary peritonitis.
- May precipitate hepatic encephalopathy in preexisting liver disease.
- Intrahepatic arteriovenous (AV) fistula.

Q: What are the **methods** of liver biopsy?

A: As follows:

- Percutaneous (better ultrasonography [USG] guided).
- Transjugular.
- Laparoscopic or laparotomy (if done for other reason).

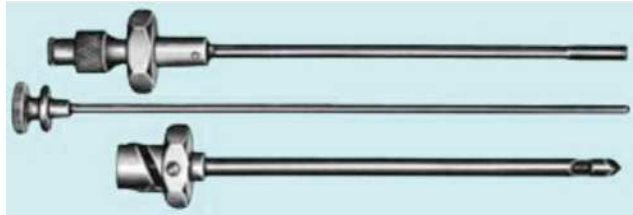
Q: What are the **indications of transjugular liver biopsy**?

A: It is done if there is massive ascites, coagulation abnormality or a small, shrunken liver.

N.B. Remember the following:

- If bilirubin is high ($>3 \text{ mg\%}$), biopsy specimen should not be taken, as the liver tissue does not take stain.
- If prothrombin time is prolonged, it can be corrected by vitamin K 10 mg daily for 3 days.
- Fine-needle aspiration cytology (FNAC) under USG guidance is more preferred nowadays.

INSTRUMENT 04: PLEURAL BIOPSY NEEDLE



Q: What is this **instrument**?

A: Abrams pleural biopsy needle.

Q: What are its **parts**?

A: As follows:

- The outer part with a cutting groove into which tissue is taken.
- A solid stylet.
- A cutting trocar.

Q: What is the **procedure**?

A: Pleural biopsy specimen should be taken during aspiration of pleural fluid with this needle. Under local anaesthesia, the needle is introduced after giving a small incision through the skin at the intercostal space. Stylet is removed and pleural fluid is aspirated. Then the cutting trocar is introduced and parietal pleura is cut. The needle is then removed, reopened and the specimen is taken out for histopathology.

Q: What are its **indications**?

A: As follows:

- Malignant pleural effusion.
- Tuberculous pleural effusion.
- Pleural effusion of an unknown aetiology.

***N.B.** In tuberculosis, AFB is positive in pleural fluid in 20% of cases and pleural biopsy is positive in 80% of cases. In malignancy, pleural biopsy is positive in 40% of cases (may be up to 60% of cases).*

INSTRUMENT 05: ASPIRATION NEEDLE WITH RUBBER TUBE



Q: What is this **instrument**?

A: Aspiration needle with a rubber tube.

Q: What are its **parts**?

A: Wide-bore needle with a rubber tube.

Q: What are its **uses**?

A: Aspiration of pleural fluid, ascitic fluid, pericardial fluid, liver abscess etc.

N.B. If aspiration needle is not available, aspiration can be done by a wide-bore blood-set needle connected to any rubber tube, which is connected to an empty saline bag. Fluid comes out easily by negative suction.

PLEURAL FLUID ASPIRATION

Q: What are the **sites** of aspiration of pleural fluid?

A: It is usually done through the sixth intercostal space in the midaxillary line or eighth intercostal space in the posterior scapular line. Clinically, it should be done at the site of maximum dullness.

Q: What are the **indications** of pleural fluid aspiration?

A: As follows:

1. Diagnostic: To diagnose the cause of pleural effusion (tuberculosis, malignancy).
2. Therapeutic:
 - Massive effusion, especially with severe respiratory distress or cardiorespiratory embarrassment.
 - Introduction of drugs such as talc, kaoline, tetracycline etc. for chemical pleurodesis (to prevent recurrence of effusion or pneumothorax).
 - Introduction of bleomycin in malignant effusion.

Q: What are the **complications** of pleural fluid aspiration?

A: As follows:

- Iatrogenic pneumothorax (hydropneumothorax).
- Infection may cause empyema.
- Acute pulmonary oedema.
- Injury to neurovascular bundle.
- Vasovagal attack as a result of fear or severe pain (pleural shock).

Q: How to avoid injury to **neurovascular bundle**?

A: The needle should be inserted near the upper border of the lower rib.

Q: How to avoid **acute pulmonary oedema**?

A: To avoid pulmonary oedema, more than 1 L of fluid should not be removed.

N.B. Remember the following:

- *If more than 1–1.5 L of fluid is taken out or fluid is taken out very rapidly, there may be pulmonary oedema. It results from rapid expansion of the compressed lung that causes leakage of fluid from the pulmonary vessels.*
- *If the patient complains of cough or respiratory distress or tightness of the chest, aspiration should be stopped.*
- *After aspiration, a check X-ray should be done to see the amount of fluid or any development of pneumothorax.*

Q: What are the causes of **failure** of aspiration of pleural fluid?

A: As follows:

- Faulty technique.
- Encysted effusion (in such a case, USG- or computed tomography [CT]-guided aspiration is more preferable).
- Thick fluid such as empyema.

Q: What should be done after aspiration of the **pleural fluid**?

A: As follows:

- Physical character: Colour (clear, straw, haemorrhagic, purulent, chylous).
- Gram staining, cytology (routine) and exfoliative cytology (malignant cell).
- Biochemistry: Protein, sugar (simultaneous blood sugar, protein and lactate dehydrogenase [LDH] may be done).
- Culture and sensitivity (C/S).
- AFB and mycobacterial C/S (in some cases).
- Adenosine deaminase (ADA).
- Other tests according to suspicion of cause (amylase, cholesterol, LDH).

ASCITIC FLUID ASPIRATION

Q: What is the **site** of aspiration of ascitic fluid?

A: At the right iliac fossa, just outside the spinoumbilical line or at the flank.

Q: How much fluid can be removed?

A: About 3–5 L of fluid may be drained daily.

Q: What are the **indications** of ascitic fluid aspiration?

A: As follows:

- Diagnostic: To find the cause of ascites such as tuberculosis, malignancy, infection etc.
- Therapeutic: Tense ascites causing cardiorespiratory embarrassment, resistant ascites refractory to medical therapy.

Q: What are the **contraindications** of ascitic fluid aspiration?

A: As follows:

- Bleeding disorder.
- Hepatic encephalopathy.

Q: What are its **complications**?

A: As follows:

- Hypovolaemia leading to shock.
- Infection.
- Injury to viscera.
- Hepatic encephalopathy.

INSTRUMENT 06: INTRAVENOUS CANNULA

Q: What is this **instrument**?

A: Intravenous cannula.

Q: Mention its **uses**.

A: Administration of any intravenous fluid, intravenous injection, TPN (total parenteral nutrition) and blood products.

Q: What are the **complications**?

A: As follows:

- Thrombophlebitis.
- Sepsis.

Q: What **precautions** should be taken to prevent venous thrombosis and embolism?

A: The cannula should be changed every 3–4 days. If kept for more than 3 days, heparin wash should be given.

INSTRUMENT 07: FOLEY CATHETER



Q: What is this **instrument**?

A: Bichannel Foley catheter.

Q: What are its **uses**?

A: As follows:

- Retention of urine.
- Spastic paraplegia.
- Neurogenic bladder.
- Incontinence of urine.
- Unconscious patient.
- Postoperative patient (major abdominal, pelvic or perineal surgery).
- Urinary bladder irrigation.

Q: What are its **complications**?

A: As follows:

- Trauma.
- Infection.
- Blockage of catheter.
- Stone formation, if kept for a long time.

INSTRUMENT 08: NASOGASTRIC TUBE (RYLE TUBE)



Q: What is this instrument?

A: Nasogastric tube.

Q: What are its uses?

A: As follows:

1. Therapeutic:

- Nasogastric feeding.
- Nasogastric suction (e.g., intestinal obstruction, acute abdomen, acute dilatation of stomach, postoperative).
- Nasogastric medication in a comatose patient.
- Gastric lavage (noncorrosive poisoning).

2. Diagnostic:

- Aspiration of gastric juice for gastric juice analysis.
- Aspiration of gastric fluid for toxicological screening.
- Fasting gastric lavage for AFB in a child with a suspicion of pulmonary tuberculosis.

Q: How can you test whether the instrument has reached the correct site or not?

A: By the following:

- Aspiration of gastric content.
- Listening to the sound with a stethoscope over the epigastrium made by injecting 20–30 mL of air through the tube.
- Emersion of the tube in water and looking for any bubble (which appears if the tube is in the airway).
- Also, if the tube enters the airway, the patient will cough violently.

Q: Why there is a **metallic bead** at the tip?

A: It helps in smooth passage of the tube by gravitational force. It also helps to localize the position of the tube in the stomach by X-ray.

Q: What are the **contraindications** of insertion of a nasogastric tube?

A: As follows:

- Tracheoesophageal fistula.
- Oesophageal atresia.

Q: If nasogastric tube **cannot be inserted**, what else should be done?

A: Gastrostomy tube should be inserted.

Q: What are the **complications** of nasogastric tube insertion?

A: As follows:

- Cough.
- Aspiration pneumonia.
- Haemorrhage.
- Injury.

INSTRUMENT 09: AIRWAY TUBE

Q: What is this **instrument**?

A: Airway tube (oropharyngeal tube).

Q: What is its **use**?

A: As follows:

- To maintain a clear airway.
- To prevent tongue from falling back in an unconscious patient.
- To prevent tongue bite in an epileptic or unconscious patient.

Q: What are its **complications**?

A: Injury to lip, gum, tongue, palate, pharynx, etc.

INSTRUMENT 10: ESR TUBE



Q: What is this **instrument**?

A: Westergren erythrocyte sedimentation rate (ESR) tube with ESR stand.

Q: What are the **markings** in this tube?

A: It is graduated from 0 to 200 mm.

Q: What are the **methods** of measuring ESR?

A: As follows:

- Westergren method.
- Wintrobe method.

Q: What is the **normal value** of ESR?

A: 0–8 mm in the first hour in males and 0–12 mm in the first hour in females.

Q: What are the causes of **raised ESR**?

A: As follows:

- Physiological: Pregnancy.
- Tuberculosis.
- Multiple myeloma.
- Aplastic anaemia.
- Connective tissue disorder:
 - Systemic lupus erythematosus (SLE).
 - Acute rheumatic fever.
 - Rheumatoid arthritis.
 - Polymyalgia rheumatica.
- Giant cell arteritis.

Q: What are the causes of a **very high** (>100) ESR?

A: As follows:

- Multiple myeloma.
- Giant cell arteritis.
- Polymyalgia rheumatica.
- SLE.
- Acute rheumatic fever.

Q: What are the causes of a **decreased** ESR?

A: As follows:

- Polycythaemia as a result of any cause.
- Afibrinogenaemia.

Q: What is the **significance** of ESR?

A: As follows:

- ESR has no specific diagnostic significance. However, it can support a diagnosis.
- It may indicate response to therapy and prognosis.

INSTRUMENT 11: METERED-DOSE INHALER



Q: What is this **instrument**?

A: Metered-dose inhaler.

Q: What are its **parts**?

A: As follows:

- Canister.
- Actuator.
- Nozzle.

Q: Name two important **conditions** where this device is used.

A: As follows:

- Bronchial asthma.
- Chronic obstructive pulmonary disease (COPD).

Q: Name some important **drugs** delivered through this device.

A: As follows:

- Salbutamol.
- Steroid.
- Ipratropium bromide.

Q: Name one **complication** of the use of a steroid inhaler.

A: Oral candidiasis (also husky voice).

Q: How would you **prevent** it?

A: Advise the patient to wash oral cavity after using inhaler containing steroid preparation.

INSTRUMENT 12: ACCUHALER



Q: What is this **instrument**?

A: Accuhaler.

Q: Name two **conditions** where this device is used.

A: As follows:

- Bronchial asthma.
- COPD.

Q: Name some important **drugs** delivered through this device.

A: As follows:

- Salmeterol.
- Fluticasone.
- Salmeterol plus fluticasone.

Q: What are its **advantages** over metered-dose inhalers?

A: As follows:

- This device is easier to use than conventional metered-dose inhalers, which require careful coordination.
- A numerical dose counter helps monitor the asthma therapy.
- More environment friendly.

Q: What are its **disadvantages**?

A: It may be difficult to use in young children or adults who are short of breath.

INSTRUMENT 13: EVOHALER



Q: What is this **instrument**?

A: Evohaler.

Q: Name two **conditions** where this device is used.

A: As follows:

- Bronchial asthma.
- COPD.

Q: Name some important **drugs** delivered through this device.

A: As follows:

- β -Agonist such as salmeterol, salbutamol.
- Steroid such as fluticasone.
- Combination.

Q: What are its **advantages** over conventional metered-dose inhalers?

A: Evohaler uses HFA 134a as a propellant instead of chlorofluorocarbon (CFC). So this is more environment friendly.

INSTRUMENT 14: PEAK FLOWMETER

Q: What is this **instrument**?

A: Peak flowmeter.

Q: What are its **uses**?

A: It is used to monitor the progress and treatment of the following diseases:

- Bronchial asthma.
- COPD.

N.B. Regular measurement of peak expiratory flow rate (PEFR) on waking from sleep, in afternoon and before going to bed demonstrates the wide diurnal variation of airflow limitation in bronchial asthma.

INSTRUMENT 15: AMBU BAG



Q: What is this **instrument**?

A: AMBU bag with a face mask.

Q: Name its **parts**.

A: As follows:

1. Inlet:
 - Air inlet.
 - Oxygen inlet.
2. Bag proper/rubber bag.
3. Safety valve/one-way valve.
4. Outlet.

Q: Name some **indications** for its use.

A: As follows:

- Cardiopulmonary resuscitation.
- Any respiratory distress.
- Temporarily, it can be used before intubation.

INSTRUMENT 16: TONGUE DEPRESSOR



Q: What is this **instrument**?

A: Metallic tongue depressor.

Q: What are its **types**?

A: Metallic, plastic and wooden.

Q: What are its **parts**?

A: As follows:

- Depressor part (broad part, used to depress anterior two-thirds of the tongue).
- Holding part.

Q: What are its **uses**?

A: As follows:

- Diagnostic:
 - To examine the oral cavity: Oral ulcer, cleft palate, Koplik spot etc.
 - To examine the throat: Tonsillitis, pharyngitis, diphtheria etc.
 - To collect throat swab.
- Therapeutic: Removal of foreign body from the posterior part of the tongue and throat.

Q: What are the causes of **white patch** in throat?

A: As follows:

- Acute follicular tonsillitis.
- Diphtheria.
- Oral candidiasis.
- Vincent angina.
- Agranulocytosis.
- Infectious mononucleosis.

ORAL REHYDRATION SALT



Q: What is it?

A: This is oral rehydration salt (ORS).

Q: What is its composition?

A: As follows:

Content	Amount
Sodium chloride	3.5 g/L
Potassium chloride	1.5 g/L
Trisodium citrate	2.9 g/L
Glucose	20 g/L

Water to be added: 1 L

Q: What are its indications?

A: As follows:

- Acute watery diarrhoea.
- Correction of dehydration.

Q: How long can it be preserved?

A: It can be preserved for up to 12 hours. It should be discarded after this time.

Q: What is the function of glucose?

A: It helps in absorption of sodium chloride.

Q: What are the composition of **rice ORS**?

A: As follows:

- Sodium chloride: 3.5 g.
- Potassium chloride: 1.5 g.
- Sodium bicarbonate: 2.5 g.
- Rice powder: 50 g.
- Water to be added: 1100 mL.

*'Now, this is not the end. It is not even the beginning of the end.
But it is perhaps, the end of the beginning'.*
—Winston Churchill

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